MALARIA

MALARIA

ACCORDING TO THE NEW RESEARCHES

BY

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TRANSLATED FROM THE SECOND ITALIAN EDITION
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WITH MAPS AND ILLUSTRATIONS

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TO

GIUSTINO FORTUNATO

PRESIDENT OF THE SOCIETY
FOR
THE STUDY OF MALARIA

INTRODUCTION

We owe to the Italians not only the name but also much of our knowledge of Malaria. From the days of Lancisi and Torti, not to mention the ancients, they have proved themselves eager and successful students of the subject. The fact that several of the centres of medical science in Italy, notably Rome, although themselves healthy, are surrounded by zones of malaria-haunted country, has doubtless contributed to the pre-eminence of that country in the study of malaria. This happy combination of circumstances, whilst securing an abundant supply of material, has enabled the well-trained observers to work without risk to themselves, or of interruption to their labours by disease, and in favourable climatic and technical conditions. A vast and important literature is evidence that these exceptional opportunities have been turned to good account.

Unfortunately, so far as the English reader is concerned, much of this literature is a dead letter. Englishmen and Americans who can read Italian are the exceptions. So that hitherto it has only been after a considerable interval and through indirect, or incomplete and too often inaccurate translations, that many of us in England and America have learned about the revolutionising work our Italian colleagues have been carrying on. More than one important fact has been common knowledge in Rome several years before it had percolated to London.

To many of us the Sydenham Society's translation of Marchiafava and Bignami's book 'On the Summer and Autumn Malarial Fevers,' by Dr. J. Harry Thompson and Dr. Edmonstone Charles, came as a revelation. Since the publication of this work in 1894, and in great measure in consequence, many of the profession in Britain, in the United States of America, and in their numerous tropical dependencies, have applied themselves to the study of the malaria parasite and added their quota to the common stock of knowledge on the subject. The Italians, however, have maintained their leading position, and when, two years ago, Ross's brilliant investigations placed the mosquito-malaria theory on an incontrovertible basis, they were the first to confirm his work, to extend it, and to throw themselves energetically into the hygienic measures it so plainly indicated.

Amongst other Italians Professor Celli, whose name has been so long and so honourably associated with the scientific study of malaria, on satisfying himself of the truth and practical value of the new departure, grafted a series of studies on the mosquito in its relation to malaria on to the work he was already engaged on in connection with the epidemiology of paludism. These studies, as this work bears ample evidence, have been conducted on the most rigid scientific lines. Throughout they bear the stamp of a master hand. Although in several respects they are not complete, nevertheless they are stepping-stones which may be trod on with confidence, and with the assurance that they will in time lead to the solution of the problem so many of us are straining after—the prevention of malaria. Some important points he has already solved. He has indicated clearly the direction which should be taken in attempting the solution of others; and he has set a valuable example as to the methods by which the still unsolved problems should be grappled with.

Although Italy has considerable practical interest in the malaria problem, her interests in this respect are insignificant as compared with those of Great Britain and the United States. Professor Celli's work therefore appeals to English-speaking peoples even more than to his own countrymen. The present translation accordingly cannot fail to be welcomed in Britain and America and in their tropical dependencies. It informs us fully of what the Italians have done and of what they are doing in the study, and in the prophylaxis, of malaria, and it will enable us to take full advantage of the information they have gleaned with so much labour. It will not fail to stimulate many of us to fresh efforts towards the practical application of, and to add to, the knowledge that has been accumulating in Rome during the last few years.

During a recent visit under Professor Celli's guidance to the Roman Campagna, I had an opportunity of seeing for myself one of the fields of observation described in this work, and to learn from Professor Celli's lips some of his methods and his objects. I saw the peasants whose sordid lives he describes so graphically, and I saw in operation the economic system which, together with malaria, has reduced these wretched people to what is practically a position of slavery. Professor Celli's *exposé* of this system must surely lead to obvious and much-needed reforms in the conditions of land tenure and of agriculture at present in vogue in the Roman Campagna, and to efforts directed to the improvement of the sanitary conditions under which the peasants there live and labour. Some system of gratuitous or partially gratuitous distribution of quinine by trustworthy agents, together with efforts to popularise and instruct in its use, might be attempted. The suggested deportation to healthy localities of the subjects of infective malaria would be a beneficial, though perhaps a difficult, measure. Something might be done towards the improved housing and feeding of the peasant, towards his instruction in the *rôle* of the mosquito as the transmitting agent of malaria. Such measures, combined with intelligently directed drainage and appropriate agricultural methods, would do much to mitigate, if not to remove, the blight of malaria from the Roman Campagna. The successful application of these and of similar measures advocated by Professor Celli would be an object-lesson which could not fail to lead to their general application in other malaria-cursed countries.

PATRICK MANSON.

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TRANSLATOR'S PREFACE

In presenting this translation of Professor Celli's able and philosophic book to English readers, I wish to emphasise the fact that malaria or so-called Roman fever now practically never exists within the walls of Rome at any season of the year.

My reason for doing so is that I and the other British medical men now practising in the Eternal City know only too well the erroneous opinions generally held in English-speaking countries, not only by the laity but also by the medical profession, that Rome is a very unhealthy city, and that malaria is very prevalent there during the whole year. Perhaps in this connection I may mention that during the six years I have been practising as a physician in Rome I have never seen a case of malaria in an English-speaking person who contracted the disease in this city or even in the surrounding Campagna. The explanation of the absence of malaria in Rome proper is given by the author in th[illegible] book.

I may add, for the benefit of those who may not be acquainted with another translation of mine, that Rome is now not only one of the healthiest cities in the world, but also one of the most desirable health resorts in Europe for certain forms of disease which are duly mentioned in that book.

JOHN J. EYRE.

31 Piazza di Spagna, Rome :
September, 1900.

PREFACE

THE SECOND EDITION

WITHIN five months from its publication the first edition of this book has been exhausted, and it is well, inasmuch as it had already become somewhat out of date owing to the great progress made in the fields of epidemiology and prophylaxis by the Italian Society for the Study of Malaria during the epidemic year just ended, guided by the new etiological theories.

I have much pleasure, therefore, in presenting this second edition, which contains additional and better figures, an account of the latest discoveries up to the beginning of 1900, and what I believe to be an almost complete bibliography of Roman Malaria from 1600 to the present time.

Meanwhile distinguished investigators, at the head of scientific expeditions which have been sent out to investigate this pestilence, have substantially confirmed, even when they have not mentioned it, the work of the Roman school, and when they have not confirmed it, have fallen, like Koch, into imperfect observations. Wherefore for us who live in the centre of one of the most splendid regions laid desolate by this scourge, the necessity increases of continuing our labours, always enlarging the field of investigations in practice, and bringing the aid of the new theories to these unfortunate people, who, true and noble martyrs and heroes, lose their health and frequently their lives for the benefit of others.

On our part, to enable us to continue our work, we again appeal for a little help to the very few who have already given it, to the very many who have not felt it their duty to interest themselves in the study of a problem which concerns a large part of the economic life of their families and of the whole nation.

A. CELLI.

ROME: *January* 1, 1900.

PREFACE

TO

THE FIRST EDITION

In the scholastic year just finished I have brought to a close the course of Epidemiology with fourteen lectures on Malaria according to the New Etiological Researches.

These lectures, more or less, with their special physiognomy and didactic structure, I have for various reasons decided to publish.

It is time, I believe, that the ancient wisdom of an epidemiological doctrine, nowadays accumulated by virtue of popular tradition and medical observation, be united and harmonised with the modern investigations.

And as to-day not only has the epidemiology of this infection been much cleared up, but, as a legitimate consequence, its prophylaxis also can and ought to be better directed to its supreme scope, I hope this book will be useful in enabling doctors to quickly put themselves *au courant* with the new studies, in order that they may know how to combine and diffuse their preventive and curative counsels in relation to a disease unfortunately so universally prevalent.

The public administrations also, and in general all those who in various parts of the world are so frequently engaged in an unequal struggle with this up till now implacable monster, ought to direct their powers towards the new horizons which international science has been able to disclose within these last years.

It is well also that in a brief synthesis we at length can understand and value what our medical school has done for the study of Roman malaria from the days of Lancisi to the present moment.

And, in fine, I am pleased to take this first occasion to express my sincere gratitude to the Italian Society for the Study of Malaria, which has furnished the means necessary for the various new researches that give character to this book.

I must also thank my assistants Dr. Del Pino and Dr. Valagussa—the former for taking down these lectures as they were delivered; the latter for having prepared the designs of the many figures which richly illustrate the text.

May these pages diffuse the impulse for the further study of such an interesting argument, even in malarious regions not yet thoroughly explored;

and in the present competition of the most civilised nations for combating such a homicidal scourge may they likewise demonstrate that, as the Italian medical school has known in the past how to fulfil its duty, so it intends to perform it in the future.

ANGELO CELLI.

ROME: *July* 15, 1899.

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PART I

EPIDEMIOLOGY

HISTORY OF THE EPIDEMY

History of malaria.—One can truly say that malaria is connected with the economic and political life of the people who inhabit the regions where it dominates, and yet the historians, as a rule, have not given and do not give it all the importance it deserves. We find it barely mentioned in the description of some wars: thus, for example, it has been said that during the invasion of Hungary by the Germans, and of Holland by the English, the invaders encountered the greatest obstacle in malaria, which decimated their armies, but spared the native troops. Many other human events and conditions are influenced by the presence of this disease, and there is no doubt that in a large measure the greater activity and progress which are to be seen in Northern Italy, as compared with Southern Italy, are due to the prevalence of malaria in the latter region. The extensive landed properties, for instance, were and still are in reality an effect of the same cause; and the celebrated phrase of Pliny, *Latifundia Italiam perdidere*, can be translated into this other, 'Malaria has ruined and is ruining Italy.' It is even to-day the most insurmountable obstacle to colonisation and, in general, to the acclimatisation of the European race in tropical and subtropical climates.

In the course of ages what vicissitudes has this epidemy undergone in Europe?

While, as a rule, one can say that it has been decreasing in the regions of the North, in those of the South, on the contrary, there has been little or no diminution. In London, when Sydenham wrote (1666–88), the pernicious fevers were anything but rare; nowadays even a case of mild tertian or quartan is very seldom seen within the confines of the great metropolis. Torti in 1712 described in Modena, where he practised, all the most classic forms of pernicious fever; to-day in that city cases of malaria are very rare, and they are of a mild form. At Turin in 1864 there were fifty deaths from pernicious fever, while to-day every trace of malarial fever has disappeared therefrom. Frerichs in 1865–6 described, in Silesia, morbid changes in the liver produced by the most severe malaria, which now is very mild there.

In Northern Europe, in England, in Germany, and in France, as in Northern and Central Italy, examples of vast and successful schemes of agrarian sanitation are numerous, while unfortunately not one can be cited from Rome down to the most southern parts of Italy, where for centuries no marked permanent amelioration in the prevalence of this epidemy has taken place.

We shall speak in due course of the wonderful conquests man has effected over malaria; here we shall sketch briefly the history of Roman malaria in the various epochs.

Pre-Roman epoch.—Colossal drainage works were executed by the first inhabitants of Latium.

In the Roman Campagna, beneath a thin layer of humus, the hills are constituted principally of volcanic tufa which being finely porous retain the rain-water; hence the permanent humidity of the subsoil. To remove this humidity and to obtain drinking water the ancients excavated for hundreds of kilometres a network of tunnels, the greater part the height of a man. Di Tucci, the engineer, and Professor Tommasi-Crudeli some years ago described them. Figure 1 shows a portion of a hill pierced by these tunnels, or drainage in three levels, which collected at the bottom of the hill the subsoil water that filtered through the tufa, and which certainly must have been used as potable

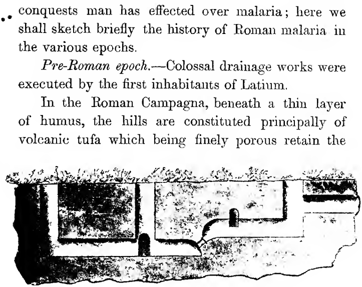


Fig. 1.

water: in fact, in the second level of the canals, in a constriction which communicates with the lowest level of this drainage, a filter has been found, that is (fig. 2) a thick slab of perforated lead, which is the earliest example of the employment of a filter in the history of our Western civilisation. Other hills have a similar drainage in two levels, or in one only.

By these and similar drainage works malaria in the Agro Romano must certainly have been much attenuated, because, in places which afterwards became deserted and have remained so up till to-day, there arose and flourished, through the work of the first Latin settlers, *Lavinium*, *Laurentum*, *Gabii*, &c., and through that of the Etruscans, *Falerii*, *Veii*, *Capene*. It could not, however, have been abolished, inasmuch as the worship of the goddess Fever was here a very ancient custom and widely diffused. And Cicero cites the old tradition that, to found the city, Romulus selected a place *in regione pestilenti salubrem*.

FIG. 2.

Roman epoch.—In the earliest times, to dry the Velabrum (*Velabra suo stagnabant flumine*, as Propertius says) in the valley between the Capitol and the Palatine (fig. 28), the famous *Cloaca Maxima* was constructed, which was at first nothing more than an enormous drain, and as such it still exists. The ancient system of subterranean drainage was modelled on the same lines, and good examples of it still remain. Thus the city was made healthy, draining subterraneously the waters that abounded on the surface (fig. 28). But, in regard to the surrounding Campagna, Livy, after the siege of Capua, says that the Roman legionaries did not wish to return any more *in pestilenti atque arido circa urbem loco*, as was always, even then, the Agro Romano.

Doubtless afterwards, for a radius of several kilometres round the metropolis, they built, as now, villas for the patricians, and suburbs, and cultivated extensively flowers, fruit, vegetables, and instituted dairy farms and poultry yards. But that they rendered the whole of the Agro Romano absolutely healthy cannot be admitted, for in the reign of Augustus, Strabo indicated a vast littoral zone as being unhealthy, and Horace wrote that the October wind *adducit febres et testamenta resignat*; and during the journey from Rome to Brindisi, while his companions stopped a little beyond the city to partake of their collation and drink the water of the spot, he himself abstained for fear of the fever. Later on Frontinus (year 91) praises Nerva because *causæ gravioris cœli, quibus apud veteres urbis infamis aer fuit, sunt remotæ.* It is certain, however, that they were not in reality removed, inasmuch as, according to Juvenal, it was always *letifer autumnus*.

It is also certain that at a long distance from the city large tracts of land remained, as they still remain, as fields and woods for pasturage, which always has been the principal industry preferred by man on this soil. Reading the letter that Pliny wrote to Gallus concerning his villa of *Laurentinum*, and following the two ancient ways, the *Laurentina* and *Ostiense*, which he describes, we find that the Roman Campagna was then much as it is to-day, with its fields and woods, with flocks of sheep and herds of horses and cattle.

Therefore, even in the time of the apogee of the Roman power malaria was not stamped out in the Campagna. And with the decline of the Empire, and after the transference of its seat to Byzantium, malaria increased. Later on the Ostrogoths, at the siege of Rome (537), interrupting the aqueducts, and devastating the Campagna, left it in a state of desolation.

Mediæval epoch.—Foreign invasions having been suspended towards the sixth century, even here the good effects of the agrarian labours of the Benedictines were felt. Meanwhile the Church, which had become master of the whole territory, divided it into six *patrimonies* (*patrimonium Appiæ, Labicanum, Tiburtinum, Tusciæ, Sabinum, Urbanum*). Each of these patrimonies was inhabited and cultivated, and for this purpose was subdivided, as Tomassetti has shown, into *masses, domocultæ, colonies*, and *hamlets*.

The *masses* were habitable centres or rural towns. The *domocultæ* were agrarian institutions, each of which contained several farms variously cultivated, and had a considerable collection of habitations surrounding a church, sometimes a group of small villages on the site of the ancient inhabited centres.

The *agricultural colonies* arose on the ruins of the ancient villas, and especially in the suburb that was richest in these ruins.

The *hamlet* was a large farm cultivated by private initiative, and had had so many habitations and such importance that twenty farms of the Agro Romano are still known by their names.

The history of the *domocultæ* deserves to be more thoroughly studied, because even to-day it would be difficult to find a system more suitable for the colonisation of our Campagna.

Pope Zachary (741–752), requiring corn, founded the first five *domocultæ*, which were built on ancient inhabited sites. Adrian I. (772–775) restored some of the aqueducts and founded other *domocultæ*. There were, according to Tomassetti, ten of these in the Roman Campagna, along the principal ways; according to others, they were twenty and even twenty-nine. Around each the Campagna was cultivated by settlers and given in feud to the convents and the Roman nobility. For a certain time a part of the products were given to the poor. This system was maintained in spite of the Lombard invasion (756), and yielded only to the destructive incursions of the Saracens (846–876), after which period the *domocultæ* were enclosed and fortified with towers. The colonies were also fortified, while, with the same object of defence, Leopolis was built at the Vatican, Laurentiopolis at San Lorenzo fuori le Mura, Johannipolis at San Paolo, Gregoriopolis at Ostia. These latter two towns were subsequently destroyed by malaria.

Meanwhile the barons summoned from the

Castelli Romani into the plain established fortified places with towers (see fig. 31) to oppose the continuous incursions of the Saracens, and finally made themselves masters of all the territory. Here, with the predominance of feudal militarism and the consequent neglect of agriculture, the prolific mediæval agrarian period ceased, and the land from that time till to-day has remained in the hands of a few rich owners. The incessant incursions of the Saracens, and later the invasions of the Hungarians (924) and of the Normans (1017), as well as the eternal wars between the nobles and with the Popes, kept the Campagna a desert, frequented only by the shepherds who descended thither in the winter with their flocks from the mountains of Abruzzo.

Modern epoch.—Contrary to what has frequently been stated, several attempts at agricultural improvements were subsequently made, but unfortunately without result. Sixtus IV. (1471–84) issued an edict that permitted any person whomsoever to till those lands where at least a third part had not been cultivated by the proprietor, who received compensation from the tiller, which was fixed by judicial experts. This arrangement was subsequently confirmed by Julius II. (1503–13), Clement VII. (1523–34), and Alexander VIII. (1689–91), for a radius more or less distant from the walls of the city. Paul V. (1605–21), besides having improved the Tiber by reopening the canal of Fiumicino, to induce the proprietors to adopt close culture, authorised the bank of Monte to advance them money at a low rate of interest, and he undertook to transport into the Agro the Moors who, expelled from Spain, went to settle in Africa. And Clement XI. (1700–21) went so far as to lend the agriculturists money without charging them any interest.

Towards the end of the eighteenth century, Pius VI., while he associated his name with the drainage of the Pontine Marshes (already attempted with some success by Leo X., Sixtus V., Innocent X. and XII., and Clèment XI.), in 1783, ordered, together with the new census of the Agro Romano, that every year a certain extent of land should grow corn.

In 1798 the Republican Government in Rome promulgated laws for the populating and cultivating of the deserted Campagna. And afterwards, in 1801 and 1802, Pius VII., to remedy the scarcity of corn, enacted agrarian laws, truly Jacobinical, decreeing fines and rewards. He taxed heavily those whose lands remained uncultivated, and with the profits arising from this taxation he helped those who subdivided their land for the purpose of having it brought permanently under cultivation by agriculturists, and he exempted them from service. This led to the formation of villages and scattered homesteads. To the colonists he also conceded rewards in money for each tree they planted, *dots* for their daughters, payment for the bringing-up of orphans and foundlings, exemptions from litigations, ready and gratuitous medical assistance. And because the unhealthiness of the air and other causes rendered the cultivation of the distant lands more difficult, he very reasonably began by imposing the new taxes on those who, within a reasonable period of time, had not cultivated the farms situated within a kind of milliary circle round Rome.

But all these laws remained a dead letter, as subsequently was the case with the edict issued by the triumvirates of the Roman Republic, by which the crown lands were given in emphyteusis to the families of the peasants who wished to cultivate them. Political vicissitudes, the omnipotence of private property and its concentration in a few hands, the absence of efficacious hydraulic sanitation, all tended to damage or destroy the provident dispositions of the agrarian laws in every age.

The various tentatives made by private individuals were also fruitless. It would be very useful for some one to write a precise history of them; I confine myself to mentioning the extensive works, now nearly all abandoned, for the irriguous cultivation of several valleys, and some of the attempts at colonisation. For instance, in the second half of the seventeenth century, when John Baptist Doni published (1667) his able work *De restituendu Salubritate Agri Romani*, the Borghese family put into practice his wise counsels at Pratica, the site of Lavinium, one of the above-mentioned inhabited centres of antiquity, where they constructed a village and brought thither families of agriculturists from the Marche and Tuscany, to whom they granted suitable farms in perpetual emphyteusis and at a very moderate rental. These families went thither in numbers and undertook the cultivation of the farms with ardour. Piazza, in the beginning of the eighteenth century, found 130 families there, while Nibby, the archæologist, when a little more than a century later he visited Lavinium for the purpose of describing the topography of the environs of Rome, states that he found there barely twelve permanent families. The Sacchetti family also endeavoured to put in practice Doni's proposals, establishing near Ostia a colony of Tuscan peasants, all of whom soon died from malaria. In the following century (eighteenth) similar attempts, of which we have testimony in the mansions still existing at Castel Fusano and Cervelletta, had a like result; the same can be said for other tentative experiments made during the present century.

After 1870, under the impulse of Garibaldi, laws were made and important works instituted for the straightening and embanking of the Tiber, for the drainage of the Agro Romano, and for the agrarian improvements within a radius of ten kilometres from the *Milliarium Aureum* around the city—notably the works of drying the ponds at Ostia and Maccarese and of the hydraulic connection of all the basins of the vast Campagna. But, unfortunately, the hygienic improvements in respect to malaria were very few. And we can also affirm that, in the districts of intense and severe malaria, the attempts at reclaiming, undertaken from the most ancient epoch up to our day, owing to the interruptions of the works or to their being badly executed, or to the enormous intrinsic difficulties, ended by being almost all fruitless. This specially applies to the sanitary conditions of the Agro Romano, which, in respect to malaria, have been little or not at all improved by what has been done there during the last quarter of a century.

Geography of Malaria.—If we cast a glance over a map illustrating the geographical distribution of malaria, we immediately see that a great part of the world is affected with this pestilence, which, in respect to latitude, reaches the isotherm + 4° in the northern hemisphere, and in the southern, on account of the marshy lands and favourable temperatures, it extends to about the isotherm + 16°. Between these two isotherms, the low-lying grounds, the plains at or below the level of the sea, and the basins of the large rivers are nearly all malarious.

Even in Europe malaria is much diffused. The lower basins of the rivers in the Iberian Peninsula; the western coasts and the valley of the Rhone, in France: the Netherlands; some parts of the Rhine valley, the mouth of the Elbe, the Baltic coast in Germany; the regions of the large rivers which discharge into the Caspian Sea, the Sea of Azof, and the Black Sea, in Russia; the basin of the Danube; the rivers and valleys of Thrace, of Thessaly, and of Greece, are all malarious.

In Italy various *malarial maps* have been published, one by the Direction of Statistics, on the basis of the mortality from this disease in the communes of the kingdom; and two on the basis of the morbidity along the railway lines.

The first was compiled by Raseri. In it, unfortunately, the zones completely free from malaria are very few; in fact, one can say, speaking generally, that 63 provinces out of the 69, and about 2,823 communes out of the 8,258, with eleven millions of inhabitants, are exposed to this scourge.

Across our peninsula it is known that the isotherm + 15° divides the temperate from the warm climate. The distribution of malaria in Italy is also divided by the same isothermal line: to the north of it the disease is rarely seen and is mild in character; to the south the disease is common and severe.

Sicily, in many of its coasts and valleys, is ruined by this pestilence.

Sardinia is so devastated by it that we can say the problem of this island is the problem of malaria.

Following the line of the coast, one sees malaria commencing at the Venetian *laguna* and extending to the mouth of the Po; from there it follows the littoral of Ferrara and Ravenna, is interrupted from Rimini downwards—not completely, however, inasmuch as malarial zones are met with in the mouths of some of the rivers, and sometimes also in their lowest valleys. Malaria reappears higher up, and becomes continuously more severe along the southern coasts of the Adriatic, and then runs along those of the Ionian and of the Tyrrhenian Seas. However, along the shores of the Gulfs of Salerno and of Naples it ceases; but again at Pozzuoli the dreadful scourge recommences, and extends through the Pontine Marshes, the Agro Romano, the Tuscan

Maremma to Viareggio. The Ligurian littoral is healthy.

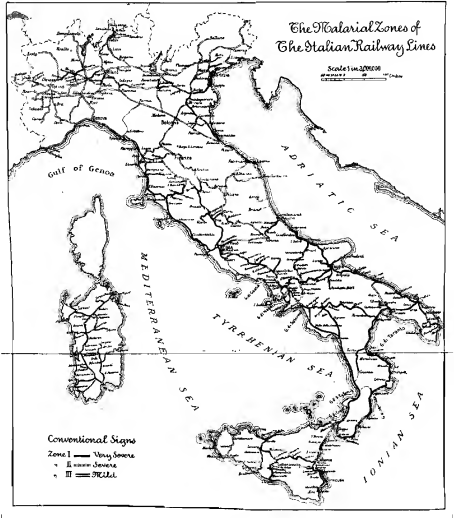
From the coasts entering into the continent we find that the valleys of many rivers, including the principal ones, such as the Po, Tiber, Garigliano, Ufanto, are all more or less malarious.

We have, then, two maps of malaria along the railway lines, where, as is readily understood, it is easier to obtain exact sanitary statistics of the railway *personnel*, inasmuch as they get an indemnity for malaria and medical attendance. One of these maps was published with a report made by Senator Torelli on malaria along the railways in Italy; the other was compiled by myself from the official data of the railway administrations (fig. 3).

The two maps are more or less in agreement. In both malaria is distinguished, and subdivided into mild, severe, and very severe.

Nevertheless, this classification must be altered, inasmuch as to-day, scientifically, we can admit only two categories, that is, mild malaria (spring quartan and tertian) and severe malaria (æstivo-autumnal fever).

We have, besides, the malarial maps of certain provinces, namely, of Capitanata and of Basilicata; that of Calabria is being prepared, and that of the province of Rome—compiled according to a type of monthly statistical bulletins, which for ten years have been sent as postcards by the parish doctors (*medici condotti*) to the prefecture—has been published by Santori. In a similar bulletin (see Table I.) are rapidly


The Malarial Zones of
The Italian Railway Lines
Scale 1 in 3,000,000
Conventional Signs
Zone I Very Severe
" II Severe
" III Mild
Domodossola
Varallo
Novara
Milano
Torino
Chivasso
Pinerolo
Asti
Saluzzo
Bra
Alessandria
Voghera
Tortona
Novi
Cuneo
Ceva
Genova
Savona
Bergamo
Lecco
Como
Brescia
Sondrio
Chiavenna
Belluno
Verona
Mantova
Cremona
Lodi
Pavia
Piacenza
Parma
Modena
Bologna
Ferrara
Rovigo
Padova
Venezia
Vicenza
Treviso
Udine
Ravenna
Rimini
Pistoia
Lucca
Pisa
Livorno
Firenze
Spezia
Ancona
Roma
Napoli
Foggia
Taranto
Catania
Siracusa
Gulf of Genoa
ADRIATIC SEA
MEDITERRANEAN SEA
TYRRHENIAN SEA
IONIAN SEA
G. di Taranto
G. di Gaeta
G. di Napoli
G. di Salerno

noted day by day, month by month, with a few strokes of a pen or pencil, the cases of *primary, recurrent, and pernicious fevers.* The recurrent fevers have to be considered apart, in order more distinctly to ascertain the course of the epidemy in the various months of the year, which can be exactly indicated only by the primary fevers. To avoid mistakes, it is necessary, however, that these primary fevers should not be confounded with the recurrent fevers with long intervals.

These, if the data be not very accurately obtained, may very easily simulate the primary fevers. Consequently, since 1888 I have adopted a criterion which to-day I have still greater reason to maintain—this is, that one must reckon as recurrent every case of fever which repeats itself in the same individual from the July of one year to the end of June of the following year, or during all the cycle of the same yearly epidemy. It is true, perhaps, that some of the consecutive attacks may be also due to a new infection in the same patient, for example, when the æstivo-autumnal fevers are seen to follow the spring forms, or when the tertian passes into the quartan; but still in such cases a mixed or double infection may have occurred at the beginning, and in the relapses one species of malaria is extinguished, the other survives. So that, all things considered, by reckoning the recurrences by the method I have mentioned, a minimum of error results.

One must also note separately the sub-continued fevers, so as not to ascribe to malarial infections the

TABLE I.—MONTHLY STATISTICAL BULLETIN OF MALARIAL FEVERS.

Commune of . *Month of*

CASES OF MALARIAL FEVERS

Days	Primary	Recurrent	Pernicious		Place where the infection was supposed to be contracted
			Sub-continued	Complicated	
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					
16					
17					
18					
19					
20					
21					
22					
23					
24					
25					
26					
27					
28					
29					
30					
31					

Medical Attendant, . *The Mayor.*

so-called sub-continued typhoid forms, which in reality are cases of typhoid fever.

When, however, one wishes to sketch a map of malaria without all these distinctions, it will be sufficient to note the distribution of those mosquitoes that, as we shall see, are the source and carriers of this infection.

Nevertheless, the maps already published are very useful, because they demonstrate the frightful diffusion of the malarial scourge in Italy, attract the attention of the public authorities to the urgent necessity of providing a remedy, and, when this is done, give the most certain mode for estimating its salutary effects.

From time to time in the various localities where malaria is endemic, the disease becomes epidemic and even pandemic; this occasionally occurs in places where it had not been prevalent for some time. We had an example of this in the province of Rome in the year 1879, when a true malarial pandemy raged.

From the statistics of the causes of death, from 1887 onwards, the following table is compiled :

Table II.—Mortality from Malaria in Italy.

1887	1888	1889	1890	1891	1892	1893	1894	1895	1896	1897	1898
21,033	15,987	16,194	15,147	18,190	15,531	15,301	15.296	16,464	14,017	11,947	11.378

ECONOMIC LOSSES

The foregoing figures tell us that the mean mortality from malaria in Italy is about 15,000 victims per year, a number which in these latter years tends to diminish, but it is still very high when we remember that it is a disease for which there is an efficacious specific remedy, and the mortality from which is therefore very low—as it was, for example, in 1896 here in the hospitals of Rome, being 7·75 per thousand of the patients suffering from malaria. Calculating from the number of deaths the number of patients, we arrive approximately at about two million cases a year. The mean duration of a malarial infection, which usually recurs, is generally long. On occasions it may continue for years. The loss of labour and of production, and the expenses entailed in dealing with this disease, consequently amount to several millions of francs. If we add that the average life of the worker in malarious places is shorter, and the infant mortality higher, than in healthy places, we get a somewhat proximate idea of the financial losses that this scourge causes to our country. Because, if we calculate that, owing to malaria, about 5,000,000 acres of land and very many localities, as, for instance, the Agro Romano, remain not uncultivated but certainly imperfectly cultivated, the economic loss derived from it must undoubtedly be enormous.

The great railway industries also feel it very much. According to the very accurate calculations of Ricchi, the Adriatic Railway Company alone, for 1,400 kilometres of railways and for 6,416 workmen in the malarious zones, spends, on account of malaria alone, the large sum of 1,050,000 francs a year.

The army in its turn, from 1877 to the end of 1897, has had more than 300,000 (about 322,678) cases of malaria.

Finally, a certain correlation exists between emigration and malaria in the sense that the regions where this pestilence is most prevalent (Basilicata, Calabria) are those which contribute most largely to permanent emigration.

To sum up, one can therefore positively assert that *malaria annually costs Italy incalculable treasure.*

ETIOLOGY

The etiology of malaria presents very special characters that differentiate this disease from all the infective diseases of bacterial origin.

It is not easy to form a clear conception of the conditions which relate to the etiology of this disease unless we enter to some extent into the fields of zoology and comparative anatomy, because we are in the presence of a parasitism produced by the class of *Protozoa* and more especially of an order of this class called the Sporozoa.

Order of Sporozoa.—These parasites are represented by true and proper cellular elements, which consist of protoplasm, a nucleus, a nucleolus or karyosoma. They have the characteristic of living at the expense of other cells, that is, of being true endocellular parasites or cytophages. They have also an amœboid phase of life, during which, in the absence of a cell wall, they are animated by characteristic protoplasmic movements. In fine, they multiply by spores, hence their name.

There are many interesting species of this order of *sporozoa*, which is subdivided into various suborders; but we shall only mention those which will give us a clear idea of malarial parasitism.

To the *sub-order of Microsporidia* belongs a sporozoon which in the silkworm is the cause of the disease called pebrine.

Cornalia first discovered it, and it is after him that certain corpuscles were named. These are nothing but spores of an oval form, endowed with great refrangibility and provided with a resistent capsule which, at complete maturation, opens and permits an amœboid body to escape, which, once free, acquires a round form, and multiplies by dividing into spores, and these, in their turn becoming free, recommence the parasitic life in the epithelial cells of the walls of the stomach of the silkworm. This evolutionary cycle is sufficiently simple. Other parasites of this order live in *Arthropoda*, for example, in mosquitoes, and in fishes.

To the *sub-order of Sarcosporidia* belong those sporozoa which complete their parasitic life in the substance of striated muscle-fibre. We, however, know only one phase of their life history, that in which they present themselves as saccules full of spores which have the form and name of falciform corpuscles. But what happens to these corpuscles, and what the antecedent and final phases of their development may be, are still little known.

We know that such endomuscular parasitism is very common in the frog, sheep, hog, and ox; in this latter animal it is called Miescher's corpuscles, which by their structure are easily differentiated from *Trichina spiralis*.

Of these sporozoa those which appertain to the *sub-order of Coccidia* are of most interest to us, both because they give rise to infections (coccidioses) not only in domestic animals (rabbit, cat, mouse, ox), but also in man (thirteen cases—some of these are doubtful, and two fatal), and because their study has opened the path to the modern knowledge of malarial parasitism.

As early as 1882 R. Pfeiffer found in these *Coccidia* a dimorphism, or an alternating generation, with two evolutionary cycles: the one endogenous and asporular, which determines the reproduction in the tissues of the hosts; the other exogenous and sporular, which permits contagion and ensures the conservation of the species. It was Schaudin, Simond, and Siedlecki who subsequently described very exactly these two cycles of life.

To fully understand them it is necessary to familiarise oneself with the special zoological nomenclature that is employed.

The cells of the protozoa which have the faculty of uniting are called *gametes*. These gametes are already differentiated into two sexes: the larger gamete, or macrogamete, represents the ovule or the ovoid as it is called; the smaller gamete, or microgamete, represents the spermatozoon or the spermoid. The cell from which the microgametes are derived is called microgametocyte; the female and the male, that is, the ovoid and the spermoid, fecundating, form a zygote from which the resistent cystic stage is derived, so that in all the coccidia the sexual phenomena precede this stage. This zygote is converted into a cyst (sporocyst) which in its turn becomes filled with spores (sporoblasts), from which the sporozoites, that is, the cells capable of recommencing the endocellular parasitic cycle, are derived.

And now we shall follow briefly the first researches of Schaudin on the *Adelea* (fig. 4 A–E)

The parasite which is found within an intestinal cell begins to undergo modifications: the karyosoma or nucleolus of the nucleus breaks up, and the

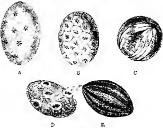


FIG. 4.

chromatin is diffused in the protoplasm, so that many centres of chromatin are formed (fig. 4 A). The cell protoplasm subsequently divides up and arranges itself around these centres of chromatin (fig. 4 B). Finally each of these particles becomes an elongated falciform corpuscle with a nucleus and protoplasm, and thus (fig. 4 C) a body is formed by a mass of these corpuscles which are the macrogametes. The cells that produce the microgametes, or the microgametocytes (fig. 4 D-E), develop in a perfectly analogous manner

Thus both may, without leaving the intestine of their host, re-enter a cell of the intestinal parietes and recommence their parasitic life separately and respectively as macrogametes or microgametes.

This is the asexual, or, as it is also called, asporular cycle of life and of multiplication.

As we shall see, the hæmosporidium of malaria likewise completes its asexual or asporular cycle within the red blood-corpuscle of man, while it attains its other more complete or sexual or sporular cycle in the body of the mosquito.

This second cycle of Schaudin can also be studied in the *Adelea*, and has been thus described: a sexual act takes place, analogous to that which occurs in the higher animals; the microgamete, or the male element, gains entrance to the macrogamete, or female element, and fertilisation results. Only one microgamete can enter the macrogamete. In the zygote or body that results from this fecundation—as is well seen in the genus *Klossia*—numerous centres of chromatin are observed (fig. 6 A), around which the protoplasm is distributed in as many spores, which are enclosed by a species of membrane and represent the resistent forms or sporoblasts;

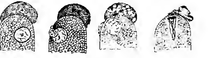


Fig. 5.

that is to say, they are true spores, which may take on an extra-cellular life, until lodging, for example, in the intestinal tube, they emit the sporozoites

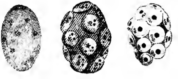


Fig. 6

that penetrate the walls of the cells of the host and recommence their endocellular parasitic life.

Schaudin has observed other very interesting facts relative to fecundation in another coccidium

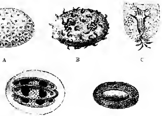


Fig. 7.

belonging to the genus *Eimeria* (fig. 7 A–E). In this genus there is also seen a polynuclear body, bristling with many nuclei loaded with chromatin. From these we pass to the formation of very motile protoplasmic bodies (fig. 7 B) that are the spermoids; one of them penetrates (fig. 7 C) the ovoid, and from the fecundated gamete or zygote are subsequently formed cysts containing the falciform bodies which represent the sporoblasts (fig. 7 D–E).

Similar facts have been more accurately studied

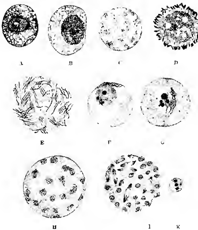


FIG. 8.

by Siedlecki in another coccidium, the *Klossia octopiana* (fig 8 A–K). This coccidium, within the cell where it lives, usually undergoes division of its karyosoma (fig. 8 A–B) into numerous minute bodies, and the chromatin is distributed in as many centres (fig. 8 C); in each centre nuclei are formed, which develop into a mass of spermoids (fig. 8 D–E). On the other hand, from the original cell, other cells are differentiated that represent the ovoids which subsequently will be fecundated (fig. 8 F–G). A spermoid enters the ovoid; the entire cell mass becomes filled with many centres of chromatin (fig. 8 H), from which, and from each one of which, bodies are formed that represent the spores (fig. 8 I). That is, one has finally the formation of a cyst containing falciform corpuscles (fig. 8 K) or sporoblasts which subsequently form the sporozoites. From these latter recommences the phase of intracellular life in which the two gametes ensure the life of the parasite only within its host.

On the contrary the phase of life that begins with fecundation and terminates with the formation of sporocysts, sporoblasts, and sporozoites, is more resistent, and more complete, inasmuch as it is that which ensures the conservation of the species in the environment and permits the diffusion of the contagion.

Having understood these few zoological facts that have thrown so much light on the study of the etiology of malaria, we shall now proceed to study the parasites of this disease, which Metschnikoff in 1887 intuitively perceived were closely related to the coccidia, and which were more correctly described by P. Mingazzini as appertaining to a special sub-order of sporozoa that are called the Hæmosporidia.

Sub-order of Hæmosporidia.—The general characters common to the sporozoa of this sub-order were defined by myself and Sanfelice in the following manner :—

1. Life at the expense of the red corpuscle.

2. Cellular structure, with a nucleus provided with an abundant quantity of chromatin.

3. In the blood a cycle of life is subdivided into two phases: the one phase endoglobular, which undergoes endogenous multiplication by gymnospores or amœbulæ or sporozoites without previous encystment; the other phase that ends by becoming free in the plasma. From this latter phase is initiated, as we shall see, the cycle of sexual life within a dipter or an acarus.

4. Marked inoculability from animal to animal of the same species and variety.

Among the distinguishing characters we note the reduction or non-reduction of the hæmoglobin into melanin, the stage of amœboid activity more or less clear and persistent, the duration of the life-cycle in the blood; and we can also add the manner in which the life-cycle is completed in the definitive host.

The sub-order of hæmosporidia is subdivided in its turn into two families, these into genera, and these genera into species. As, however, the genera and species are not yet complete, and the various names may cause confusion, I prefer to speak of the different kinds of malaria met with in various animals, indicating for each the diverse parasites up to now found in their blood. We begin with

MALARIA OF BATRACHIA AND OF REPTILES

We take, for example, the hæmosporidium of the frog (*Rana esculenta*), first studied by Danilewsky.

Figures 9 A–E show the principal stages, first described by us, of the endoglobular phase that terminates with multiplication by gymnospores.

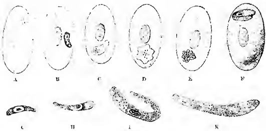


Fig. 9

Figures 9 F–K show the other phase, already known by the name of *Drepanidium* (Ray Lankester, Gaule), within the red corpuscles or free in the plasma. They have a vermicular movement, and enlarging, elongate themselves.

Which in this latter phase are the macro- and microgametes, and in what definitive host the life of these hæmosporidia continues and is completed, we do not yet know.

MALARIA OF BIRDS

The first researches of this infection in similar animals are also due to Danilewsky.

While the parasites of the red corpuscle in cold-blooded animals reduce the hæmoglobin very little, and, in general, do not destroy the red corpuscle, those of birds, on the contrary, and still more, as we shall see, those of man, nourish themselves at the expense of the hæmoglobin, converting it into melanin, and thus finally destroy the red corpuscle itself.

In the pigeon (*Columba livia*) there is up till now only one well-known parasitic species, whose

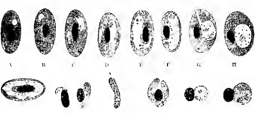


FIG. 10.

development is rather slow (fig. 10 A–P), requiring at least eight days for its completion. Small, roundish, immobile forms of a palish grey colour, without pigment-granules, first appear in the red corpuscle: they immediately begin to elongate, frequently showing a constriction, generally in the middle, resembling the figure of 8 (fig. 10 A–C). Still elongating, they lie ordinarily at the side of the nucleus in the direction of the long axis of the red corpuscle, and acquire granules of coarse black pigment. When the parasite has attained its greatest size it occupies more than half of the corpuscle and bends round the nucleus, even sometimes surrounding it (fig. 10 D–H). Frequently, however, when the whole of a red corpuscle round the nucleus is invaded, it consists in reality of two or three parasites which, growing, have come into contact with one another (fig. 10 I). The phase of endoglobular life must terminate with asexual multiplication; this, however, is not yet fully known. Beside the endoglobular

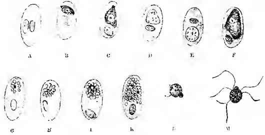


FIG. 11

forms there are the gametes or the free forms (fig. 10 K–P) in the plasma, which are frequently seen attached to the nucleus, the residue of the destroyed red corpuscle. Some of these free forms emit flagella or spermoids.

In the lark (*Alauda arvensis*) the parasites (fig. 11 A–M) have a rapidity of development and a size intermediate between those of the ringdove and those—as we shall see—of the screech-owl. They reside at one of the poles of the red corpuscle, and tend at once to become spherical. The asexual multiplication (fig. 11 G–K), and also the gametes, which emit flagella, can be readily observed (fig. 11 L–M).

In the screech-owl (*Athene noctua*), besides a parasitic species very similar to the preceding, another is found (fig. 12 A–O) with small forms and rapid development, in which asexual multiplication quickly takes place (phase of endoglobular life), while other forms (fig. 12 I–M) enlarge within the red corpuscle and then become free (phase of free life, or of the gametes), and some of them emitting flagella or spermoids (fig. 12 N–O).

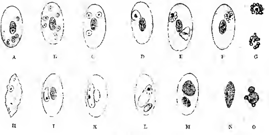


Fig. 12.

The parasites of the red corpuscle are observed in the blood of other birds (sparrow, starling, owl, &c.), than the pigeon, the screech-owl, and the lark. All, however, can be referred to one of the three above-described species of hæmosporidia: it is not possible, therefore, to accept the classification made by Labbé into two species only, *Proteosoma* and *Halteridium*.

These hæmosporidia of birds have another life-cycle that is completed in the body of another animal, which Ross has discovered to be the mosquito. In the blood of birds we see the first of the cycles that have an asexual method of reproduction; but of the second we see only the initiation of what we call the phase of free life; that is, we see the formation of the bodies which, with Grassi and Dionisi, we call microgametocytes, because they emit flagella or spermoids, and of other free bodies that do not emit flagella and are macrogametes or ovoids. Already in the blood of birds fecundation of the ovoid by the

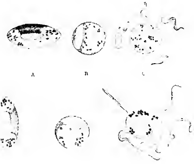


Fig. 18

spermoid can be detected. Such fecundation was first observed by MacCallum (see fig. 13 A–F). This author has distinguished the female forms or macrogametes from the male forms or microgametocytes; the former (fig. 13 A–C) are a little cloudy, refractile, and contain fine pigment granules; the latter (fig. 13 D–F) are almost hyaline, and contain coarse pigment granules; from these protrude flagella or spermoids, one of which the author has seen penetrate and fecundate a macrogamete (fig. 13 C).

After this fecundation the second life-cycle of the hæmosporidia of birds commences. Major Ross, of the Indian Medical Service, at the suggestion of Manson, the celebrated parasitologist, who had already described the life of the filaria in the body of the mosquito, made mosquitoes (*Culex pipiens*) bite infected birds, and by systematically dissecting a mosquito each day, of those which had bitten the birds, he discovered the phases of the life-cycle of the hæmosporidia in that insect.

We shall now proceed briefly to describe the development of what we may call the cycle of Ross (fig. 14 A–F). On the first day there are only the free forms, many of which have protruding flagella. It is very probable that if fecundation has not already taken place in the body of the bird, it takes place now between the spermoids and the ovoids in the middle intestine of the mosquito. On the second day (fig. 14 A) these forms become more spherical and begin to show a capsule, that is to say, they are transformed into cysts. The contents still show pigment; vacuoles and refractile granules appear in the protoplasm. On the third day (fig. 14 B) the vacuoles and the refractile granules increase; on the fourth day (fig. 14 C) the cysts appear larger, the vacuoles have increased in number, and the granules of pigment are still seen. Successively (fig. 14 E–F) the cysts continuously enlarge, the so-called vacuoles become larger, some round, others ovoid; in the protoplasm there remain undivided bodies called *residual nuclei* or *nuclei de reliquat*.

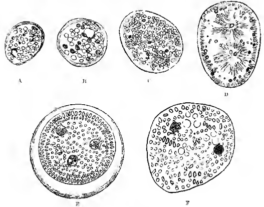


Fig. 14.

Between the fourth and the sixth days Ross gives a figure (fig. 14 D) which should have been put last, inasmuch as the vacuoles are elongated in the form of sporozoites.

Ross has not described the final stages of development so accurately as it has since been followed in the mosquito infected with human malaria. He has however observed sporozoites in the salivary glands of the mosquito, and has seen that the infected mosquitoes infect healthy birds. He has thus arrived at the discovery, confirmed by Koch and by us, of the transmission of malaria to birds by means of mosquitoes. To sum up, the perfect hæmosporidium is that seen in the mosquito, which therefore represents the definitive host of the parasite, while the bird is the temporary host, because in its blood the asexual life only of the above-mentioned hæmosporidium develops.

MALARIA OF MAMMIFERS

The first hæmosporidia of this form of malaria were found in *oxen*. In the places where human malaria prevails, especially severe malaria, there also exists bovine malaria which attacks preferably imported breeds, but at the same time does not altogether spare the indigenous ones.

In the Agro Romano it is a very old disease, which was formerly confounded with hæmorrhagic infections, and particularly with anthrax; and it is only lately that it has been identified by us as malaria. Owing to the frequency of hæmoglobinuria in the Roman Campagna, it is vulgarly called *pisciasangue* (bloody urine). The symptoms of the infection are high fever and hæmoglobinuria, and these are followed by death, which sometimes occurs, in a large percentage of cases, in a very short time.

Jaundice is also frequent This disease may decimate or even completely destroy a herd of milch cows. It is transmissible by the inoculation of blood from cow to cow; not, however, to other animals.

Babes first, and later and more accurately Smith and Kilborne, described in the red corpuscle a rather small pear shaped parasite (fig. 15 A–K), frequently coupled in pairs, hence the name *Pirosoma bigeminum* given to it by these latter authors. We have also seen it undergoing amœboid movement, less active, however, than in the æstivo-autumnal hæmosporidium of human malaria. Its multiplication is difficult to see in the circulating blood; some authorities believe that they have discovered it in the capillaries of the cardiac muscle, but we have not succeeded in finding it there. Besides this grave and frequently fatal acute form there is a mild winter form, with a protracted course, which is more difficult to diagnose clinically, as there is no fever nor hæmoglobinuria.

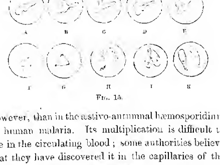


FIG. 15.

In a case of this kind by staining preparations in a special way (*see* Part II.—'Verification of the Diagnosis'), we have seen that one of the two endoglobular bodies, frequently ring-shaped, is stained blue and the other near it is stained pink: possibly one has to deal with two forms already sexually differentiated, namely, the two gametes.

Smith and Kilborne have demonstrated that this malaria is transmitted to oxen by the bite of a special tick, the *Ripicephalus annulatus*, which is about the size of the head of a pin, and, after biting an ox and sucking its blood, becomes very large, falls off and subsequently lays an egg. The daughter ticks are capable of transmitting the disease, infecting other cows with their bites. This has been clearly demonstrated by Smith and Kilborne, and also confirmed by Koch. This tick, which is the definitive host of the hæmosporidium of bovine malaria, is found everywhere in the countries where this disease prevails; that of the Roman Campagna is identical, according to Grassi, with that found by Smith and Kilborne in America.

In *calves* Kolle has found other endoglobular parasites, somewhat different from the preceding.

In *sheep* there is a form of malaria due to a parasite which was described by Bonome and called *amœbosporidium*. In fact, it has an amœboid stage more evident than that of bovine malaria, and also shows clearly the asexual multiplication in the circulating blood.

I have observed a form of malaria also in the *young lambs* of the Roman Campagna. It is known to the shepherds that young lambs, feeding in marshy places, are subject to a severe and fatal anæmia, which by analogy we may call malarial. Indeed, in the blood, parasitic forms are found that closely resemble those of bovine malaria. That it is possibly identical may be assumed from the fact that a calf which was placed in a stall where one of these lambs lay dead, after eight days fell ill and died of the same infection. Moreover, in the Roman Campagna they say that bovine malaria is contracted where diseased sheep have been feeding. In sheep, therefore, there are very probably two species of malaria: the one of the bovine type, and the other of the type described by Bonome.

Piana and Galli-Valerio have described a form of malaria in *pointers*, and especially in those dogs which go from healthy places to hunt in malarious irrigated meadow-lands. In the Roman Campagna it has also been observed that the sporting dogs which come from Lombardy become infected.

The parasite of this malaria of dogs is endowed with active amœboid movement, but it assumes a pyriform shape, so that it resembles the parasite of bovine malaria.

Possibly *horses* also are subject to malaria, especially those brought from healthy places. Certainly febrile reactions have been described in horses, that begin with a rigor and end with sweating. Precise observations of the blood of these cases are, however, still wanting.

Lastly, Dionisi has discovered and described in *pipistrels* diverse malarial parasites, which most nearly resemble those of man. Thus he has distinguished two large pigmented forms, which finally invade almost all the red corpuscles, and resemble the hæmosporidia of the tertian and quartan fevers of man; and a third, smaller and non-pigmented variety, which resembles some of the æstivo-autumnal forms of man, that is to say, it presents itself as small white spots containing particles of hæmoglobin which have not been converted into melanin. These three forms have such a slow cycle of evolution that it is difficult to follow it to sporulation; the gamete phase is, however, very distinct and persistent in the lethargic period. The definitive hosts of these parasites of sheep, dogs, and bats are not known.

In the monkeys of Africa also, Koch has found endoglobular parasites, more recently described by Kossel.

Endoglobular parasiticism is, consequently, very diffused in the animal kingdom, from the batrachia to man.

HUMAN MALARIA

It is known that Laveran made the first fundamental discoveries of the parasites of malaria in November 1880. They, however, were not accepted by the scientific world until Marchiafava and I had demonstrated that the melanin which is characteristic of this infection was formed within the parasite, and had pointed out the resemblance which these bodies have in amœboid movement and cell structure to the protozoa, and that they multiply by fission. Golgi subsequently demonstrated their cycle of endoglobular life in tertian and quartan fevers, and we demonstrated it in the severe æstivo-autumnal forms, in relation to the febrile period. We defined exactly, from the clinical, epidemiological, and parasitic points of view, the two fundamental groups of fevers, namely, the mild or spring fevers, and the severe or æstivo-autumnal fevers. And, together with Sanfelice, I defined precisely the intimate analogies which exist between all the parasites of the red corpuscle in their life within the blood, from the batrachia to man.

We know to-day also that the hæmosporidia of malaria of man, like those of birds, have two life cycles: the one asexual in the blood of malarial beings, the other sexual in the body of special mosquitoes.

The various hæmosporidia, so long as they are in the blood of man, possess the following characteristics: active amœboid movement; cellular structure, that is a nucleus and karyosoma in the fresh preparation, and abundant chromatin demonstrated by special staining (*see* Part II.: Verification of the Diagnosis); inoculability from man to man, in the sense that the experimental inoculation of malarial blood from man to man always reproduces the fever, except in some rare case, when, as we shall see, one is dealing with an individual immune against this infection.

As in birds there are at least three species of these parasites, and in sheep two, so in man there are two for the mild fevers, and one at least for the severe or æstivo-autumnal forms.

The spring quartan and tertian parasites give rise to the mild forms; the æstivo-autumnal tertian, and, more rarely, the æstivo-autumnal quotidian, which is also called true quotidian, to distinguish it from that pseudo-quotidian which results from a double tertian or a triple quartan, give rise to the severe forms.

The spring forms of the parasite are characterised by their slow development in the red corpuscle for two or for three days, according as to whether they are the tertian or quartan; by the large size they attain in the red corpuscle, being able to occupy all or almost all of it; by the abundant pigmentation which appears early; and by the fact that the entire asexual life-cycle, from the invasion of the red corpuscle to the multiplication by fission with formation of gymnospores or amœbulæ, can be followed in the circulating blood. Both the tertian and the quartan parasites also present the life-cycle, which eventuates in the presence of large pigmented bodies free in the plasma, which in man are unable to proceed to their final stage of development, but are the beginning of a further phase of life, that is, the sexual life-cycle which is completed in the mosquito, and are now called gametes. In man these free forms have a nucleus which is sometimes visible even in the fresh preparations; some of them emit filaments that formerly were called perfect parasites by Laveran, flagella by us, agonic forms by Grassi and Feletti, and now are called microgametes or spermoids. Those which emit these spermoids are the male free forms or microgametogens or microgametocytes: the microgamete or spermoid fecundates a female free form or macrogamete

We now follow Golgi in some morphological details.

The *quartan* parasite has the following principal characteristics (fig. 16 A–K):—

1. It completes its asexual life-cycle (fig. 16 A–H) in three days (72 hours).

2. It invades nearly the whole red corpuscle, but does not enlarge or discolour it, even when it has almost entirely filled the corpuscle.

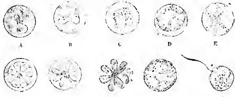


Fig. 16.

3. The amœboid movement is rather sluggish; the form does not change much while under observation. The contours of the hæmosporidium are readily distinguished from the rest of the red corpuscle.

4. The pigment consists of coarse granules. The granules have feeble movements.

5. Towards the end of apyrexia the pigment collects in the centre, and fission or formation of the amœbulæ begins. These (fig. 16 G–H) are from 6 to

12–14 in number; frequently, when the pigment is in the centre, the amœbulæ are arranged round it in a daisylike form.

The principal characteristics of the *spring tertian* parasite are (fig. 17 A–K):—

1. It completes its asexual life-cycle (fig. 17 A–H) in two days (48 hours).

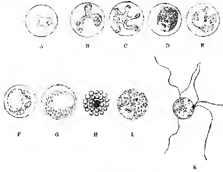


Fig. 17

2. It invades the whole of the red corpuscle, which becomes enlarged and pale. Frequently it is rather difficult to differentiate the contour of the parasite from the edge of the red corpuscle which surrounds it, because the red corpuscle is so pale that it has almost lost its hæmoglobinic tint. So that one may mistake it for a free form, while still endoglobular. The loss of colour of the red corpuscle takes place when the parasite is still small.

3. The amœboid movement is very active; the changes in form of the parasite are quite apparent, and, while watching it, pseudopodia can be seen to be rapidly protruded and retracted.

4. The pigment consists of fine granules which move actively.

5. Towards the end of apyrexia, the pigment tends to collect in the centre, and multiplication begins. The number of amœbulæ is generally greater than in the quartan, consisting of from 12 to 20 (fig. 17 H).

As a differential characteristic between the parasite of the spring tertian and of the quartan one also observes that the gametes of the tertian (fig. 17 I–K) are much larger than those (fig. 16 I–K) of the quartan. It is probable that slight differences exist also in the final development which takes place in the body of mosquitoes.

The parasitic forms that give rise to the severe æstivo-autumnal fever are principally those of the *æstivo-autumnal tertian*, which has been well differentiated from the mild or spring tertian by Marchiafava and Bignami and confirmed by Koch.

The æstivo-autumnal hæmosporidia (fig. 18 A–V) are very different from the spring ones; they are much smaller, occupying, as a rule, not more than a fifth or a quarter of the red corpuscle. They have very active amœboid movement. The pigment consists of very fine, almost invisible granules.

The parasite also changes its position in the red corpuscle, and disappears and reappears out of focus, according to whether it sinks down or rises to the surface of the red corpuscle. From the stage of active movement the parasite next passes to the stage of rest, presenting a discoid or an annular form; in this case it presents itself under the

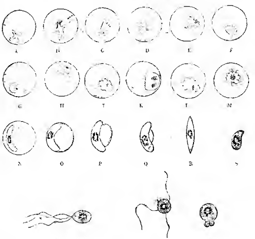


Fig. 18.

latter form, which is pretty distinctly seen in the bottom of the red corpuscle. It completes its asexual life-cycle (fig. 18 A–M) in 48 hours. To follow the whole of this cycle of development is, however, more difficult than in the spring forms, because the parasite, when it has reached the phase of multiplication, collects in the internal organs, where fission into amœbulæ or gymnospores takes place.

In the circulating blood, however, one sees sufficiently often, whatever Koch may say, the round pigmented forms, with scattered granules, and a particle of black pigment in the centre, which precede fission, but the fission forms are hardly ever seen; so that to see the entire asexual life-cycle it is necessary to puncture the spleen during life, or examine the blood of the spleen, liver, bone-marrow, or cerebral capillaries after death. In cases of comatose pernicious fevers, which are the most frequent with us, we find the capillaries of the brain full of these parasites, pigmented or in fission; sometimes not a single red corpuscle in these capillaries is spared. It gives rise to a true parasitic thrombosis of the cerebral capillaries, the observation of which readily explains the severe cerebral symptoms that we see in many cases of pernicious fevers (comatose, soporous, bulbar, apoplectic, meningitic, &c.).

This form of tertian is also called malignant, inasmuch as it may become malignant, the paroxysms being prolonged and approaching one another till it simulates a continued fever and becomes sub-continued; it is also called æstivo-autumnal tertian, because it is observed only in the summer and autumn, never in the spring. Indeed, it is known among us that the spring fevers never give rise to a pernicious fever. A double tertian, or a triple quartan may give rise to at most the apparently quotidian fevers with anticipating attacks, but never to pernicious fevers.

Only the æstivo-autumnal fevers, therefore, if they be not treated early, become pernicious.

In the æstivo-autumnal tertian some forms are also observed in the blood, very rapidly altering the red corpuscle, which becomes shrivelled, spinous, smaller, and of a darker colour than the others—similar to that of old brass. It is an early necrosis of the red corpuscle, which has lost its elasticity. To these altered corpuscles, each of which contains an æstivo-autumnal parasite, Marchiafava and I have given the name of *brassy* (*ottonati*) *red blood-corpuscles*, to indicate their colour. This early necrosis of the red corpuscle demonstrates the greater perniciousness of this parasite towards the red corpuscle.

The red corpuscles, in æstivo-autumnal fevers, may be altered or destroyed by hæmolysis even without being invaded by the parasite, and then one sees that grave symptom hæmoglobinuria, which is very frequent in severe tropical malaria, rarer in the Roman Campagna, where, as we have seen, it is more commonly met with, in the malaria of other mammifers.

In this æstivo-autumnal tertian, while the life-cycle that leads to asexual multiplication develops (fig. 18 A–M), other forms (fig. 18 N–V) appear, which become the so-called crescents of Laveran, that is parasites of a crescentic shape with nucleus and with the pigment collected in the centre. It is sufficient to see one of these crescents to be certain that one has to do with an æstivo-autumnal fever. They may become ovoid, fusiform, or round. Some of the round forms emit flagella, which Grassi and Dionisi now call microgametes or spermoids; these are always less numerous than in the free forms or microgametogens of the spring tertian.

A lengthened discussion has taken place concerning the significance of these crescents. Canalis believed he had seen them in sporulation, which, however, was only the vacuolisation of the protoplasm. In 1889 I and Guarnieri demonstrated their abundant chromatin, and I compared them to the falciform corpuscles of coccidia. These forms may remain in the circulating blood and in the blood spaces of the viscera—that is, in the spleen, and especially in the bone-marrow—for whole months, without being febrigenous, even when the endoglobular forms of the parasite have disappeared. In the human organism, therefore, they appeared to be, and in fact are, sterile.

Besides some of the crescent bodies, Guarnieri and I have described certain minute bodies, that we can now compare to the polar corpuscles which are emitted before fecundation, it being known that in the reproduction of the protozoa a part of the chromatin of each gamete is expelled before conjugation.

But it is only since the latest studies on the coccidia that the true signification of these crescents, and of the flagellated bodies which are derived from them, has been fully understood. Here, also, we can now say, we have female and male forms, the macro- and micro-gametes: the latter or spermoids are the flagella that are emitted by the above-mentioned bodies of the crescent phase; the macrogametes are spheres which await fecundation by these spermoids. Fecundation may, as in birds, occur in the blood of man after extraction; but it certainly takes place in the stomach or middle intestine of the mosquito that has sucked human blood containing the hæmosporidia of this phase.

In fresh preparations the young forms of this sexual cycle, or the young crescents, are, according to Bastianelli and Bignami, the size of a non-pigmented amœba with a distinct contour, and a strong and very characteristic refrangibility; the pigment disseminated or massed has always, however, the typical needle-shaped appearance, which is seen in the adult crescents.

By special staining the protoplasmic body is stained a more intense blue at its periphery, and the pale central part contains the chromatin in the form of minute rods more or less near one another. These, with the growth of the crescents, increase in number, while the pigment collects towards the centre, hiding the part containing the chromatin, or the nucleus. They are afterwards differentiated into the two sexes.

The male bodies, that is, those which emit microgametes or spermoids or flagella, become round, their nucleus does not exhibit a definite outline, the chromasomes or nuclei migrate to the periphery of the parasite, and from each of them originates a long thin filament; the protoplasm also takes part in the formation of the spermoids surrounding the filament of chromatin, so that the microgamete or spermoid consists of a thread of chromatin surrounded by a halo of protoplasm.

The female bodies or macrogametes, on the contrary, preserve the crescent or spindle-shaped form longer; the chromatin is less in amount, is situated in the centre of the nucleus, and has the shape of a granule; the nucleus is surrounded by the pigment, and the protoplasm is stained a darker blue. So that the special staining also tends to demonstrate the diverse function these two species of crescent bodies possess.

In conclusion, this hæmosporidium of severe fevers also has, as we have seen to be the case in the hæmosporidia of birds, and in the hæmosporidia of the spring fevers, two cycles of development, that is, one asexual, in the blood of man, the other sexual in the middle intestine of special mosquitoes.

That the quartan, the spring tertian, and the æstivo-autumnal tertian are distinct parasitic forms can also be demonstrated by the inoculation of malarial blood from diseased man to healthy man. The inoculation of a minimum dose of malarial blood, much less than a drop—even a puncture made with the needle of a Pravaz syringe stained with malarial blood, is sufficient to reproduce not only the fever, but even the febrile type together with the species of hæmosporidia which is inoculated. According to Bastianelli and Bignami this constancy of species is maintained and recognised also in the body of the mosquito during the cycle of sexual life of the hæmosporidia.

In the summer and autumn one may have, though it is rare, a true quotidian, or an æstivo-autumnal corresponding to a parasite very similar to that of the æstivo-autumnal tertian, but completing its cycle of development in twenty-four hours. This form is described as being smaller still than the tertian form, with granules of pigment which are scarcely visible.

There is also another parasitic form which Marchiafava and I have very rarely observed, and it has been confirmed in tropical climates by Marchoux; it develops very rapidly—in less than twenty-four hours—and is non-pigmented, but it proceeds to multiplication without having first converted the hæmoglobin into melanin. It is the form which has been called *Hæmamœba immaculata* by Grassi and Feletti.

Between tropical malaria and the malaria of our warm climates there is no substantial difference; the parasitic forms which multiply without producing pigment, and which give rise to hæmoglobinuria, have also been observed among us. Still more closely, according to Koch, the tropical fevers of German Africa resemble our æstivo-autumnal.

The malaria of cold climates is distinguished from that of hot climates, because in it only the mild quartan and tertian prevail or are observed, which among us are, as we have said, chiefly seen in the spring.

A well-known characteristic of malarial fevers is the liability to *recurrences* (*recidive*), which may persist often for months, sometimes for a year, and even longer. How are these recurrences explained? It is difficult to say; perhaps they depend on forms resulting from asexual multiplication, that remain inert in some viscera—possibly in the bone-marrow—and from time to time, invading anew the blood, give rise to new generations of the asexual cycle. Both in mild and in severe fevers, one can have recurrences even at long intervals—after three or four months and more. Sometimes in the intervals in the æstivo-autumnal fevers, the crescents are observed in the circulating blood, even in cases which have been treated with big doses of quinine, so that Golgi had erroneously believed that these crescents represented the germ of recurrent fevers with long intervals. The spring fevers also have a tendency to recur for a long time, and with such long intervals, even of several months, that they mimic the primary infections.

It is certain, then, that patients suffering from æstivo-autumnal malaria can contract mixed infections; and as, in the course of the winter and spring recurrences, the first to disappear are the severe fevers, we find, in those places where in the summer the æstivo-autumnal fevers only prevail, in the spring they are no longer seen, or the fevers only prevail, which for this reason precisely we have *a potiori* called spring fevers.

Two other fundamental and characteristic facts are observed in malarial infections: one is acute *anæmia*, more or less severe, which is due to the great destruction of the red corpuscles produced by the endoglobular parasites, and consequently is observed especially in æstivo-autumnal fevers. In the spring forms, on the other hand, it develops slowly, either because, as a rule, the parasites are fewer, or because they do not exercise such a destructive action on the red corpuscle as those of the severe fevers, in which many corpuscles are destroyed even without being invaded by the parasite, perhaps by an exaggerated hæmolytic power of the blood-serum.

The other characteristic fact of malaria is *melanæmia*, with the consecutive *melanosis* of the viscera, which depends, as we have demonstrated, on the conversion of the hæmoglobin into melanin by the active work of the parasite within the red corpuscle.

The *febrile period* coincides, more or less, with the endoglobular life-cycle of the parasite in the sense that the rigor, or the febrile onset, coincides more or less with the asexual multiplication, and with the discharge into the blood-stream of the gymnospores or amœbulæ.

These amœbulæ, after having invaded new red corpuscles, grow slowly during apyrexia, and prepare the new parasitic generation. If there be more than one generation of them, we shall have, for example, triple quartan, double tertian, which are pseudo-quotidian, and the fevers with paroxysms anticipating, even to subcontinuity. It still remains, however, to explain the phenomenon of fever, which in its intimate mechanism, in this as in the other fevers, is altogether unknown.

And how can the *perniciousness* of the severe fevers be explained? We cannot always attribute it to the large number of parasitic forms. And then more than ever arises the question: During endoglobular life do the parasites produce toxic substances, which are more toxic in the æstivo-autumnal and especially in the pernicious fevers than in the spring fevers? Certainly the dissolution on a vast scale of the red corpuscles even of those not invaded by the parasite, the formation of the brassy red corpuscles, which are corpuscles necrosed directly the parasite invades them, and the acute nephritis that sometimes arises during severe malarial infection are facts which speak for a greater toxicity of the parasite of the severe fevers.

But can this malarial toxin be demonstrated, and is the fever really due to it, as those authors believe who speak unreservedly of a *pyrogenic toxin*?

This is an important question, both as regards the pathogenesis of malarial infection and prophylaxis. The febrile attack may be explained by the production of toxin, and the critical defervescence by the production of antitoxin. And inasmuch as where there is toxin one can likewise obtain antitoxin, one may attempt an antitoxic prophylaxis and therapy.

There are some authorities who admit this toxin, because it explains sufficiently well many facts which are observed in malarial infection; others believe that they have seen a proof of it in the augmented urotoxic coefficient in the urine of malarials; but this urotoxic power can increase in the urine in any febrile or non-febrile state—for example, in muscular fatigue—by the greater quantity of waste products which are eliminated with the urine, and which have nothing to do with toxins.

For the demonstration of these toxins direct experiments, however, are necessary. Therefore we have searched for a pyrogenic toxin, bleeding oxen affected with malaria during the onset of the fever, obtaining the serum from the blood, and inoculating large quantities—60–90 c.c.—in very small healthy calves. And we have succeeded in producing only a very slight or no rise of temperature.

We have made analogous experiments also in man. Already Gualdi and Montesano, and later Mannaberg, had inoculated without effect small quantities of blood-serum taken from those suffering from malaria.

But we, during the summer and autumn of 1898, having had a large number of patients suffering from malarial fevers in the hospitals, were able to take a small quantity of blood from many of them at the beginning of the fever, and thus collected together notable quantities of the serum of malarial blood abstracted during the cold stage. We first inoculated young children with 50 c.c. of it subcutaneously, at another time another 50 c.c. intravenously.

Thinking that this quantity of serum might have been too small, we concentrated 260 c.c. of it at a low temperature, to a small volume, in the excellent *vacuumapparat* of Mürrle, and we injected it into the veins and under the skin of another little child. Not one of these serums nor 25 c.c. of serum obtained from a small bleeding in a case of very severe comatose pernicious fever produced pyrexia, but only, and that not always, a slight rise of temperature which one observes after inoculating a certain quantity of serum of a healthy person.

Consequently, up till now, *we have not been able to demonstrate a pyrogenic malarial toxin in the serum of the blood of those suffering from a malarial attack.*

This toxin may be shut up in the blood corpuscles. Well, we have centrifugalised the blood directly it was extracted from persons in the febrile period of malaria; we have collected the corpuscles from the bottom of the tubes of the centrifuge, dried, pulverised, and then dissolved them in a normal solution of salt, and inoculated the resulting solution. Again we had only a slight rise of temperature. Therefore not even within the corpuscles could we demonstrate this pyrogenic malarial toxin.

We shall now proceed to study the

CULTIVATION OF THE MALARIAL PARASITES IN THE BODY OF SPECIAL MOSQUITOES.—Man, according to Grassi and Dionisi, is the temporary host of the malarial parasite, and the mosquito its definitive host. In man the parasites may continue to reproduce themselves for months and years, but their complete or perfect life is the sexual one. This takes place in the body of the mosquito.

Several other cases are well known in which a parasite completes its entire development in two diverse beings.

It is well known, for example, that the armed tænia presents itself in the human intestine in its most perfect form, that is, the tapeworm, while its prior stage develops, instead, in the hog—that is, from the larva develops the vesicular worm which corresponds to the cysticercus. The adult form of the tænia echinococcus is found in the dog; the prior form, or echinococcus cyst, in the viscera especially of the hog, equines, cattle, sheep, and also of man.

After what has been said on the biology of the coccidia, and on the cycle discovered by Ross for one of the hæmosporidia of birds, it is easy to understand what happens to the parasite of human malaria within the special mosquitoes which are its definitive host, and which appertain, as we shall see, to the genus *Anopheles*.

Perhaps in 1897 Ross partly saw the first stages of development of the æstivo-autumnal parasites in the body of a dappled-winged mosquito. But it is Grassi, Bastianelli, and Bignami who have given us all the details of the development of the æstivo-autumnal and spring tertian parasitic forms in the mosquito, and the latter two authors also of the quartan.

It is to be premised that, in the æstivo-autumnal fevers, the formation of the gametes takes place in the bone-marrow, where one sees all the stages of development, from the very small crescents to the young. Those larger are seen in the circulating blood. The microgametocytes emit the spermoids. Within the first twelve hours, at about 30° C., in the stomach or middle intestine of the mosquito that has sucked human blood, and after the spermoid has entered the ovoid, and fecundation has been completed, zygotes are seen which result from this fecundation, presenting very varied forms, and are easily recognised by the black pigment characteristic of the endoglobular cycle which they possess.

These fertilised bodies migrate between the epithelial cells of the middle intestine of the mosquito, where they are found after forty hours; then they begin to project into the general body cavity, and finally rupture into it.

Before bursting, however, the final stages of development have taken place, which are completed in seven or eight days, in a way very analogous to what we have seen when studying the cycle of Ross.

Figures 19 A–G and 19 I–O represent the various stages of development—the first, fresh preparations; the second, stained.

They treat of forms which become continuously larger, eight to ten times larger than those that are seen in malarial blood, and they are surrounded by a membrane-like capsule.

The chromatin of the nucleus increases, divides and subdivides by direct division into many minute bodies, each of which becomes a nucleus. Around

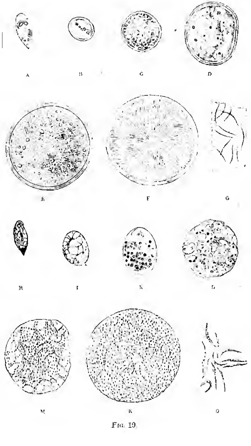


Fig. 19.

each nucleus the protoplasm divides, and one observes an enormous polynuclear multiplication of the parasite which first was unicellular. Successively the protoplasm round each nucleus elongates, and acquires a fusiform shape. Thus the formation of the so-called sporozoites takes place which (fig. 19 *a* and *o*) are elongated or fusiform bodies, perhaps not less than 10,000 in number, each of which has one or more chromatin granules in its centre.

As in the coccidia and in the hæmosporidia of birds, here also are seen the residua of segmentation of the protoplasm, or the residual nuclei or *nuclei de reliquat.*

The production of the sporozoites completed, the capsule bursts, and the sporozoites escape into the general cavity of the mosquito's body, and by the lacunar circulation they reach the salivary glands, where they accumulate in very large numbers. The mosquito, biting man, with its saliva inoculates him with a certain number of these sporozoites, which, developing in the blood of man, produce those asexual parasitic generations that we have already described.

For the spring tertian Bastianelli and Bignami maintain that the zygotes, or the forms of the sexual cycle, are distinguished, in the body of mosquitoes, from those of the æstivo-autumnal tertian. The first are differentiated by the round and non-crescentic form of the sporozoon, its transparent appearance, by the character of the pigment being identical with that of the same parasites in man, by the nuclei being less numerous and larger, by the sporozoites being less heaped, and dispersed more regularly in rays, and by the residua of segmentation being more numerous. So that this fact which is observed in the intestine of the mosquito is also in favour of the plurality of the species of hæmosporidia of human malaria. In the quartan also, according to these authors, things are very similar to those of the mild tertian.

The temperature at which the hæmosporidia develop in the mosquito's body must be above 16° C.; however, the maximum temperature is about 30° C. It is probable that those of the quartan develop at a lower temperature, but this requires further proof.

Be this as it may, it is now proved beyond doubt that *the cycle of perfect life, that by which the species external to man is assured, is completed by the hæmosporidia of human malaria in the intestine of the mosquito.*

SOURCES OF MALARIAL INFECTION

Man is an undeniable source of infection, both experimental and natural. It is known that when a healthy man is inoculated even with a very minute quantity of malarial blood, it reproduces not only this infection, but also the type of the fever with the relative hæmosporidia.

But from the point of view of the mode of natural infection, it is known that a malarial person can mix freely with other patients or with healthy individuals without conveying to them the disease; to-day, however, we must add: provided there are no mosquitoes present capable of biting him and healthy individuals.

The **mosquito**, the definitive host of the malarial parasite, is the second source of infection.

That the mosquito was connected in some way with malarial infection has been imagined, as we shall see, by many, but that it was the true source of infection has been for the first time supposed by analogy with filariasis. It is known that the English parasitologist, Manson, and later our Sonsino, had found that mosquitoes sucked blood containing filariæ at night, which develop ulteriorly in the body of these insects. These subsequently die in water, in which and with which are spread the germs of this disease to man by his drinking the infected water.

By analogy, Laveran and Manson thought that something similar happened with malaria: the mosquitoes sucked malarial blood; the parasites, still more the above-mentioned flagella which were considered as the perfect parasites, were cultivated in the body of the mosquito; this, dying, would infect water, and man drinking this water would contract the malarial infection.

This is not so in reality, as we shall see; but thus arose, though by hypothetical and not exact premisses, the idea that mosquitoes were the sources of malarial infection. After the concepts and suggestions of Manson followed the above-recorded studies of Ross in India, and then those of our colleagues Grassi, Bastianelli, and Bignami.

From the moment it was proved that certain mosquitoes were the culture medium of the malarial germs in the environment, it became undeniable that these insects shared with man the property of being, with the production of this *virus*, a source of infection, which therefore circulates, so to speak, from man to mosquito, from mosquito to man, and so on.

And here at once a very important problem arises from the epidemiological point of view: In this circulation or transmission of malaria by the work of mosquitoes is the presence of man really indispensable? What has happened originally we do not know, neither do we know how and where the parasitic chain commenced which extends from the cysticercus to the tænia.

But to-day, how does the case stand? It is said that in some islands, with many mosquitoes and other favourable malarigenous conditions, but uninhabited, this infection has developed only after the arrival there of malarial man. Certainly if malaria could be transmitted independently of malarial man, the struggle against this scourge would be much more difficult; because in such case it would be necessary to admit its hereditary transmission from mosquito to mosquito, and as long as one of these mosquitoes survived in a locality it would be able successively to infect others, indefinitely perpetuating the infection.

If, instead, a mosquito be not born infected, but is infected by solely biting a malarial person, the prophylaxis against malaria will be much facilitated, and, as we shall see, the isolation of man infected by malaria will acquire capital importance.

We have already stated that this hereditary transmission of the infection from tick to tick takes place in the malaria of oxen. Ross, in the malaria of birds, has described in the body of mosquitoes the so-called *black spores*, which he supposes to be resisting spores, the true resisting spores of the hæmosporidium of malaria; but according to Grassi, Bignami, and Bastianelli, they in reality have to do with a process that leads to the death of the parasite, that is, they are involution-forms or sporozoites or so-called residua of segmentation. Consequently they are not other parasites of the mosquito, as Ross has recently maintained.

Up till now resisting spores, developing, as in the coccidia, by sexual life, from the hæmosporidia of malaria, are not known, that is, spores which are resistent in the environment outside the mosquito.

Such hereditary transmission may, according to Grassi, occur in two ways: either the germ is undoubtedly in the egg, and hence passes to the larva, the nympha, and the adult mosquito; or the larvæ eat in stagnant waters, with the various detritus, the remains of the body of the infected mother mosquitoes, and thus they infect themselves in their turn.

Well, with mosquitoes, experiments, similar to those made by Smith and Kilborne, and later, by Koch, with ticks and oxen, can be repeated, that is, making mosquitoes born of infected mothers bite healthy men in non-malarious places; but these experiments, repeated here in the Santo Spirito Hospital and in the Laboratory of Comparative Anatomy, have given only negative results.

So that up to now neither morphologically nor experimentally is it possible to demonstrate the hereditary transmission of the infection from mosquito to mosquito, neither by the eggs, nor by the larvæ which have eaten spores. We do not as yet know resisting forms or forms capable of living in the environment, external to the body of the mosquitoes.

Where malaria exists there mosquitoes abound; but, *vice versa*, malaria does not exist in every place where mosquitoes abound. This fact has been explained by Grassi, who has undertaken an accurate study of medical zoology, searching for mosquitoes in all Italy, both in the malarious and in the immune districts; and he has demonstrated that in the malarious districts there live particular species of mosquitoes which are absent in the immune districts.

Of the European *Culicidæ* very numerous species exist, which have been described by ancient and recent authors, frequently insufficiently or confusedly. Ficalbi, Professor of Zoology in Messina, has recently brought a little more order into this chaos, rejecting many species, describing accurately others, and accepting the three genera admitted by Meigen in 1818:

the genus *Culex*, the genus *Anopheles*, and the genus *Aedes* (absent in Italy).

The differential diagnosis that most interests us, namely, that between the genus *Culex* and the genus *Anopheles*, is made from the appendages of the buccal apparatus.

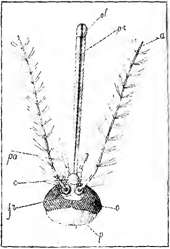


Fig. 20.—Female of Culex (after Ficalbi).

In the *Culicidæ* (fig. 20) the sting, rostrum, proboscis, or beak consists of a grooved sheath (*pr*) and terminates in a final enlargement called the olive (*ol*). Situated laterally to the proboscis are two appendages, the palpi (*pa*), and two antennæ (*a*) more or less ramified.

Now in the genus *Anopheles* (fig. 21), both in the male and female, the palpi are as long as the proboscis; while, on the other hand, in the genus *Culex* (fig. 20) the palpi in the female are much shorter than the proboscis. As generally, only the females suck blood, the differential diagnosis between the *Anopheles* (long palpi) and the *Culices* (very short palpi) is easy.

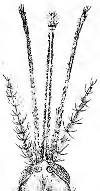


Fig. 21.

Grassi has demonstrated that the mosquitoes capable of harbouring the malarial parasite and of infecting man, belong to the genus *Anopheles*, and of this genus the mosquito, which is never wanting in malarious places, and is consequently the main cause of malaria, is the *Anopheles claviger* of Fabricius, also called *maculipennis* by Meigen, because it has on each wing four black spots arranged in the form of a capital T (fig. 22) the horizontal bar of which is partly wanting.

Thus also Grassi, Bignami, and Bastianelli have demonstrated that the *Anopheles superpictus*, the *Anopheles pseudopictus*, the *Anopheles bifurcatus* are likewise capable of cultivating and transmitting malaria; the first two especially in some parts of Southern Italy. So that in general one can say that the genus *Anopheles* is pernicious. This name in Greek means *hurtful*, and consequently it truly has been a prophetic name in zoology.

The *Anopheles superpictus* has four black spots arranged in a line along the anterior or external edge of its wings.

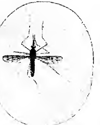


FIG. 22.

In the *Anopheles pseudopictus* the four spots are not distinctly marked: in both species between the black spots exist others of a yellowish colour.

The *Anopheles bifurcatus* has no spots in its wings.

In order of frequency after the *claviger*, which, as we have said, is never wanting in malarious places, comes the *bifurcatus*. The other two are relatively rare.

The common mosquito, and the analogous species of the genus *Culex*, which are much more diffused than the genus *Anopheles*, are the definitive hosts, and therefore the source and the carrier of the very diffused malaria of birds, but, in spite of what Koch says about them, not of that of man. That some species of *Culex*—*penicillaris* and *malariæ*, for example, which Grassi has also found in malarious places—transmit human malaria is not probable; it is likewise improbable that other insects which suck the blood of man and of other animals, such as the genera *Ceratopogon*, *Simulia*, *Phlebotomus*, do so. The extensive experiments made with this last by our colleagues up to now exclude it. The same may be said of similar experiments made with that minute insect, very common here in the Campagna before the dog-days, that is, the so-called *serapica* (midge).

It remains to be seen if also the non-pigmented species of parasite, which are rarely met with in man, more frequently in the pipistrel and other mammifers, are transmitted by the agency of the mosquito, or, as Grassi supposes, by that of an acarus.

Neither is another question, very interesting from the epidemiological point of view, definitely solved, namely: Can animals which, like the pipistrel, have hæmosporidia very similar to those of man be a source of human malaria? Dionisi, who has studied them carefully, inoculating them in man, after an incubation of 15–20 days, has seen intermittent febrile attacks arise; without, however, parasites in the blood, and, in one case, not even in the spleen. Adding some morphological differences and the impossibility of cultivating them in mosquitoes, we have sufficient evidence to say that human malaria is not connected with that of pipistrels.

It was also interesting to investigate whether in the mosquito a spontaneous cure of its malarial infection and a consecutive immunity take place by the agency of antagonistic substances or of other antagonistic parasites. Up till now, however, nothing of all this has been demonstrated.

In any case the ancient theory by which malaria was cited as being the most classic example of a disease of the soil, equal to and perhaps greater than anthrax or tetanus, has been destroyed.

The germs of malaria external to man, from what we positively know up till now, and from what we have said up to now, do not live directly in the **soil,** but in the body of the mosquito: and the soil as a source of infection takes a secondary and indirect position, inasmuch as it is favourable or not to the life and development of the malarial mosquitoes. It, therefore, now passes into the category of the indirect epidemic causes, that is to say, those which we will call respectively predisposing or immunising towards epidemics of malaria.

That the soil was not *per se* a source of malarial infection, or, in other words, that the germs of this disease do not live directly in the soil, even before these latest studies I, together with Dr Valentini, had demonstrated by the very diffused malaria of birds. If the germs of this malaria were contained in the soil in the months of the greatest diffusion of the epizootic, inoculating healthy birds with the earth of intensely malarious places would have reproduced the disease. We have experimented thus for a whole year on the ringdoves which, in malarious places, in certain months, are almost all infected. We selected nestlings that, with repeated examinations of the blood, were proved to be healthy; we kept them in a healthy place, and made very numerous injections, of earth from malarious districts, under the skin, into the veins, the peritoneum, and the trachea; but we never reproduced the malarial infection.

Also with the amœbæ cultivated from malarious soils and then inoculated in various animals I always obtained negative results.

Moreover, Silvestrini at Sassari had previously inoculated men with the soil and water of malarious places with equally negative results.

It appears, then, clearly that the hypothesis according to which it has been held by many, and is still held, that **water** is a source of malarial infection, is not supported by experiments. Even Manson and Laveran, while making the mosquito intervene, adhered to this theory. Furthermore, Laveran from the beginning firmly believed that he had found pigmented parasites analogous to those of human blood in marshy waters.

But water also, be it even marshy or stagnant, must be rejected as a direct source and, as we shall see, a direct vehicle of infection.

Water can be, and certainly is, as we shall also see, the place where the eggs, the larvæ, and the nymphæ of the mosquitoes, that afterwards become the source and carrier of infection, live. Consequently it also now takes its place among the predisposing or immunising epidemic causes.

LIFE OF THE MALARIAL GERMS IN THE ENVIRONMENT

That is to say: *the life and habits of malarial mosquitoes in the environment.* This is a new and very interesting study, which is now being followed with much activity, and was commenced long ago by Lancisi, who (Lib. I., pars 1, cap. xvi. *De noxiis paludum effluviis*, &c.) noted *culicum ingens copia in palustribus locis*, and was interested *de culicum ortu et transformatione*.

It is known that mosquitoes live only in damp and low-lying places; they pass through their respective phases of egg, larva, nympha, and perfect insect or imago. In the stages of egg, larva, and nympha they live in water; the life of the perfect mosquito is altogether an aërial one.

The genus *Culex* lays eggs which have the shape of a boat or a raft. Each boat consists of many small tubes placed side by side, from each of which is born a young larva. These boats are deposited in stagnant water, and are never found in swiftly running water: frequently they are attached to marsh plants on the surface of the water. The larvæ have a life more or less long in these marshy waters, where they live, nourishing themselves with the organic detritus suspended in the water. From each raft of *Culex* a very large number, up to 200 or more, of young larvæ are born; this fact was known to Lancisi, who in the above book describes well the development of the mosquito and the *eorun-*

dem fœcunditas mirabilis. Here among us, where the winter is mild, we always find the larvæ of *Culex* in certain waters, even when shallow, and those of *Anopheles* in deep waters. From the spring onwards we see new generations of eggs, while the larvæ are transformed into nymphæ, and these, if the surroundings be favourable, in a few days are transformed into the winged insect, leaving the nympha case in the water.

The larvæ of *Culex* are sometimes met with in enormous quantities in very muddy, and even putrid waters; when they come to the surface to breathe they occupy an oblique position, with the head downwards and the tail upwards; this is due to the fact that the single breathing tube in mosquitoes of this genus opens at the caudal extremity.

In the favourable season the whole cycle of a generation is completed in thirty to thirty-two days; and, therefore, from April to the end of September there are ordinarily four or five generations of mosquitoes. Ficalbi calculates that from a mother-stem in four generations two hundred millions may be born, and twenty milliards in five. Fortunately, however, there are natural agents which destroy them.

The aërial mosquitoes live in damp and dark places. By day they hide under bridges, in caves. cellars, stalls, woods, and trees; in the evening they issue forth into the open air, in certain places in veritable swarms, and, being hæmatophagous, attack man and other animals. In the winter very many die; a certain number, however, survive, hibernating in woods, the trunks of trees, houses, cellars, stalls, and huts, remaining immobile or from time to time biting man. Ficalbi states that in Sardinia, and especially in Sicily, they bite more or less during the whole year.

In general only the females bite and suck blood, very rarely the males.

The larvæ are phytophagous; the aërial mosquitoes in the first period of life may also be phytophagous, at other times they are immediately, or soon become, hæmatophagous.

The *Anopheles*, according to Grassi, do not lay their eggs in the form of a boat, but in the shape of a ribbon, or in many little strips (*A. claviger*), each strip consisting of from five to twenty eggs, or in stellate forms (*A. bifurcatus*) which float on the water, and on every slight movement separate.

These eggs are deposited in sequestered places, generally in stagnant, or almost stagnant, clear spring waters, where there are very few or no eggs or larvæ of the genus *Culex*. Not rarely, however, we have found larvæ of the *Anopheles* in the same place with those of the *Culex penicillaris* or *annulatus*. Sometimes, as in certain watercourses and rice-fields, those of the *Anopheles* first appeared, and then those of the *Culices*; at other times, as in a market garden, those of the *Culices* first appeared, and in enormous numbers, and then those of the *Anopheles* in much more limited numbers. In general they are found in deep waters, and when the temperature is warm also in superficial waters, always, however, in stagnant, or almost stagnant, clear waters. As a rule, the so-called ground waters, rising to the surface and running slowly (trenches or canals), or slowly renewed (lakes, marshes, ponds), constitute the best *pabulum vitæ* of the *Anopheles* larvæ.

These waters, having generally a constant temperature, are relatively warm in winter and cool in summer, and freely nourish what we shall see is the so-called palustral vegetation. The larvæ and nymphæ of the *Anopheles* are always isolated and are never found in such numbers as those of the *Culices.*

They are immediately recognisable, and are distinguishable from those of the *Culex*, inasmuch as, besides being isolated, one by one, they have a zigzag movement, and when they come to the surface to breathe they always take a horizontal position, because their breathing tubes open directly and separately on the back.

The variety of colours of the larvæ of *Anopheles* is original and characteristic.

Figure 23 shows a larva and figure 24 a nympha of *Anopheles*, both enlarged about 3 diameters. The shape resembling the point of interrogation, and the lively capers which the nymphæ exhibit in water, are known; and it is important to note the great necessity that the larvæ and still more the nymphæ have for air.

The eggs of *Anopheles claviger* at 20°–25° C. require about 30 days to become perfect insects.

These after another 20 days begin to lay eggs; so that about 50 days are required for each generation. In July and August even 40–45 days may be sufficient.

Meinert has maintained that the mosquitoes of the genus *Anopheles* have two generations annually, one in the spring, the other in the summer. When the summer is hot, there are three generations; and then both the development of new mosquitoes and the æstivo-autumnal malarial infection are prolonged to November, and even to December. Up till now, however, here among us it appears that the new generations of *Anopheles* follow one another irregularly from spring onwards, according as to whether the season is favourable or not.

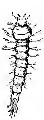


FIG. 23.

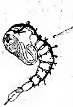


FIG. 24.

The aërial *Anopheles* may be hæmatophagous directly they are born, and after they have digested the blood they bite more than once, about every two days, and ovulate several times.

The *claviger* is domestic—that is, it lives and hibernates in houses; the *bifurcatus* is wild—that is, it lives and hibernates in woods.

The fact, for a long time known, that malaria is contracted especially in the evening and at night is explained to perfection by the habit of the blood-sucking mosquitoes of biting especially in these hours. Thus also is well explained the reason why malaria is sometimes taken in the day, sleeping, for example, in a malarious place, under a tree, or in a grotto.

Just as the larvæ have enemies—fish, for instance—so also the aërial mosquitoes have their enemies in birds, and certain dragon-flies, which feed on them; but, owing to their great fecundity, they are assured of an exuberant maintenance of their species.

Both the larvæ, and especially the nymphæ, offer notable *resistance to natural physico-chemical agents*, for example, to the *desiccation, chilling, putrefaction, saline or sulphurous condition*, and *movement of the water* in which they live. Of the studies that we are making in this connection with Dr. Casagrandi, we can already give the following results:—

TABLE III.—RESISTANCE OF LARVÆ AND NYMPHÆ (GEN. ANOPHELES) TO NATURAL AGENTS.

Agents	Maximum duration of life	
	Larvæ	Nymphæ
Desiccation at 20° C.	2 days	Survive
,, ,, 32–35° C.	1 ,,	—
,, ,, 38–40° C.	2 min.	2 min.
Earth—very dry	—	Develop
,, moist	4 days	,,
,, saturated	Survive	,,
Ice—discontinuous	48 hours	,,
,, continuous	32 ,,	24
Putrefaction—animal	36–48 hours	Develop
,, vegetable . . .	Survive	,,
Sea water	7 hours	,,
,, mixed with fresh water 2 : 1	13 ,,	,,
,, ,, ,, ,, ,, 1 : 1	72 ,,	,,
,, ,, ,, ,, 1 : 2	Survive	,,

The larvæ and nymphæ of the genus *Culex* resist all these natural agents a little longer than those of the genus *Anopheles*.

The above table shows that it is not necessary to have the soil always marshy to assure the life of the larvæ and nymphæ, an intermittent marshiness being sufficient. This is specially so for the nymphæ. We have placed these nymphæ in very dry soil, that is, the sand of the Tiber; and we have seen them almost all transformed in a few days into very active mosquitoes. Thus when the waters become shallow and the edges of the ponds or ditches remain uncovered, one has a favourable condition for the birth of the aërial mosquitoes, because the nymphæ, even if the soil become completely dry, develop in a few days into mosquitoes. This happens also in rice-fields, where, when the waters are let off for the reaping, there is in the suitable season a great diffusion of mosquitoes and also of malaria. Then if the larvæ remain in moist earth they do not by any means die immediately. In our experiments they survived for four days, and consequently they can await the water that comes to bathe them anew. In saturated soil the larvæ survive very well. On the contrary, in dry soil they die very quickly.

Ice, especially if it be continuous, is certainly destructive to the larvæ; but those larvæ which exist in clear and deep waters, where the temperature keeps relatively high, may survive with us even the whole winter.

The larvæ of *Culex* resist both animal and vegetable putrefaction for more than 72 hours, and the nymphæ develop into mosquitoes in it. The larvæ of the *Anopheles*, however, eventually die, particularly when the surface of the water is covered with a film of bacteria. This confirms the statement of Minzi, Colin, and Tommasi-Crudeli, that putrefaction in waters is not favourable to the development of malaria. It remains, however, to be seen whether the *Anopheles* cannot sometimes, in exceptional circumstances, adapt themselves to live even in muddy and slightly putrid waters. Grassi, for example, has found this unusual habitat of theirs, which Ficalbi calls foveal, very common in Grosseto, that is, in puddles and in receptacles containing dirty water, left to themselves, and we also have on one occasion found them in the muddy water of a channel in a market-garden.

Salt waters per se are certainly not favourable to the larvæ of mosquitoes. Lancisi had already seen it when '*marina aqua . . . sola seu impermixta resideat.*' In fact, the nymphæ develop even in sea water, while the larvæ, both of fresh and of sulphurous water, die there in 6–8 hours. In mixtures of fresh and salt water, on the other hand, the larvæ do not die for a long time; this to a certain extent justifies the old opinion of the Tuscan medical school, according to which malaria develops from similar mixtures. Indeed, it is remarkable that the larvæ of *Anopheles* can survive in muddy waters, even when the sodium chloride reaches 2 per cent.—that is, almost as much as sea water contains.

May they not have a progressive and gradual adaptation to living even in very salt waters? We do not yet know. For the larvæ of *Culices* it is probable, since Ficalbi found on one occasion the larvæ of *Culex numerosus* even in salines; for those of *Anopheles* an apposite study will be made at Comachio.

We know, on the other hand, through our experiments, that if the larvæ of *Anopheles* are put in *sulphurous waters*, which are such a prolific nest for those of the common mosquitoes, they succeed in living there; they, however, up till now have not been found in the sulphurous waters, the so-called Albule, of Tivoli, from which, for our various experiments, we have extracted thousands and thousands of those of the genus *Culex*. Nevertheless, they were found by Grassi in the sulphurous waters beneath Sezze, which are weaker than those of Tivoli.

The *movement of water* is hostile, as we have said, to the life of larvæ. These, therefore, attach themselves to fixed bodies or remain near the banks, where there is little or no current. Having measured the velocity of the current in the discharging canals of our Campagna, I can say that the maximum velocity of the water in a canal in which the larvæ of *Anopheles* were found was 63 millimetres per second in the centre of the current. This canal was totally free of vegetation excepting at its edges, where it was plentiful, as is always the case.

These first notions of the biology and habits of mosquitoes require to be completed; but what we know already serves to clear up much regarding the epidemiology of malaria.

VEHICLES OF MALARIAL INFECTION

Popular experience among us has given a name to this disease which is universally recognised, and which tells us that the **air** must be its vehicle. We shall see how this fact, very anciently known and undisputed, must be interpreted to-day.

But meanwhile we shall see immediately, by the light of epidemiology, what the laws are which govern the diffusion of malaria in the air.

Of the various hours of the day, it is known that the most dangerous for catching the fevers are those, as we have already said, of the night, and especially of the evening. By day it is rarely that one, if he be awake, contracts the fevers in malarious places.

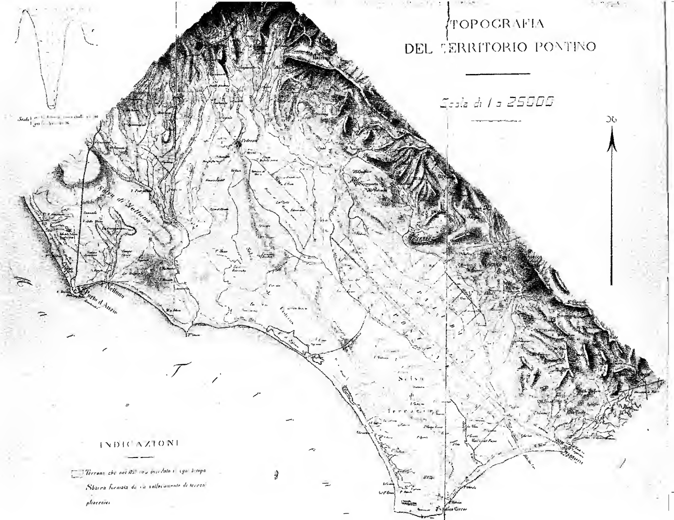
It is equally certain that a focus of malaria has round it only a limited radius of influence. That malaria is autochthonous is justly maintained by all; it is the type of the local epidemies. Baccelli has rightly said that we trample upon malaria. In the Roman Campagna there are various centres sufficiently habitable, though sometimes near notoriously unhealthy places.

From a focus of malaria can *its diffusion take place in various directions*, that is, in a *horizontal* direction, in an *oblique* direction from a low-lying place to one more elevated, and in a *vertical* direction?

There are many examples which demonstrate that malaria spreads but little in a horizontal direction. A typical example of a small circumscribed focus is that described by Marchiafava and Spadoni. Near Sinigaglia there is a canal between the River Misa and the sea; the water stagnating there was, up till a little time back, the *fomites* of malarial infection. The inhabitants of the nearest houses, and more especially of the houses with the doors and windows looking on this canal, suffered from malaria, while those of the houses a little more distant remained immune.

Even from large foci malaria is propagated only a short distance in a horizontal direction. There are many instances of ships having anchored very near intensely malarious coasts without a single person on board contracting the fevers, while those persons who went ashore and slept there were attacked. In the delta of the Tiber, at Fiumicino, a severe centre of malaria, the people of the place sleep in boats on the sea in order to avoid the disease. True ship epidemics of malaria are extremely rare, if even one can say that undoubted examples of them have occurred, in which the diagnosis has been confirmed by the examination of the blood.

Ambrosi and Riva have very recently made an accurate study of malaria in the rice-fields of the province of Parma, also in regard to the radius of influence through which this disease is spread. They found that it is diffused from a minimum distance of half a kilometre to a maximum of 4–5 kilometres, as the following table shows :—



TOPOGRAFIA DEL TERRITORIO PONTINO

Scala di 1 a 25000

INDICAZIONI

Terreno che nel 1811 [illegible] in ogni tempo

Sbarra formata da un sollevamento di terreni pliocenici

TABLE IV.—DIFFUSION OF MALARIA IN A HORIZONTAL DIRECTION.

Communes	Rice-fields	Radius of influence metres	Observations
Golese . .	Baganzola-Cervara	1,000–2,000	In a radius of 300–400 metres all the houses were attacked.
Torrile . .	S. Andrea . .	2,000	
Colorno .	Bosco . . .	1,600	
Casali . .	Fienil bruciato .	500	
	Lumaca vecchia .	800	
	Casa bassa . .	700–800	
	S. Pietro . .	[illegible]00	
	Campana . .	4,000–5,000	
Lissa . .	Campana . .	4,000	
S. Martino .	Golese . . .	4,000	

In an *oblique direction* also the propagation of malaria from a low-lying place to one more elevated is limited. A good example has been found by Tommasi-Crudeli near Girgenti, where in consequence of a marshy river there is a malarious focus close to the famous ancient temples situated below the town. The custodians of these temples who sleep in the house nearest the marsh are subject to malaria; those who sleep in a house a little further away, and in a somewhat higher position, escape the infection.

The Pontine Marshes are a vast focus of severe malaria.

Figure 25 is an excellent map of this territory. On the right is seen the zone of the Lepini Mountains; on them, and more precisely on the hills that rise above the low malarious plain, are human habitations. Those who work in the marshes go up there to sleep, faithful to the popular tradition which teaches that the best means of protecting oneself from fevers is to sleep in an elevated place.

Thus the town of Sermoneta, which is situated

257 metres above these marshes, is connected with the plain by means of a plateau that, especially on the side, gradually rises. This town, from the end of the last century up till to-day, has been literally decimated by the fevers, because under it, through an error in calculation committed in the drainage of the Pontine Marshes, the bed of a river was interrupted, and an enormous marsh was consequently produced.

In the neighbouring Sezze, which is situated on a hill a little higher (319 metres), in the summer and autumn months the inhabitants of the houses looking on the marsh are attacked by malaria, while in the rest of the town, and on the opposite slope, they are generally spared.

These are two examples of the propagation of malaria in an oblique direction, from a vast malarious focus, to a distance, however, relatively short.

In the *vertical direction* malaria is propagated only to a little height. The people who inhabit malarious places, to protect themselves from the fevers, go to sleep in trees or in beds placed on the top of four poles embedded in the soil. These elevated beds are to be seen in the Pontine Marshes and in the Agro Romano, where on the ruins of the ancient monuments one also frequently sees mediæval cottages.

A greater height from the ground is, however, necessary to escape being bitten by mosquitoes, because they, when they are very hungry, may fly to the top floor (20–25 metres) of a house.

We have an excellent example of the propagation of malaria in the vertical direction in the same Pontine Marshes. The town of Norma (fig. 25) is built on the top of a rock 343 metres high, which rises as perpendicularly as a wall, and up there the inhabitants do not suffer from the disease.

Under Norma lies Ninfa, once a flourishing town, and in the Middle Ages the seat of Papal consistories. Of that town nothing remains but the ruins and a solitary house with a mill. The people who work there are so subject to the fevers that they are obliged to be changed every week during the most dangerous months.

Consequently, *malaria is an eminently autochthonous or local epidemy, and is only transmitted to a limited distance in any direction.*

These axioms of malarial epidemiology are not in accord with certain theories which have been held for a long time in the medical schools, that is, that malaria can be transported to great distances by *winds.* Here in Rome, formerly they had great dread of the *scirocco* (south-east wind), and of warm winds generally, fearing that they transported malaria from Africa. In Sicily the strong *scirocco* brings with it some of the African sand; little wonder, it was said, is it that such winds transport the germs of malaria also, which must be very much smaller and lighter.

Many facts, nevertheless, were opposed to this theory. Tommasi-Crudeli has justly observed: 'If the winds can transport malaria from Africa across the Mediterranean, why do not malarial epidemies appear in the ships that plough the Mediterranean? Why are some towns which are heated by the *scirocco* winds immune from malaria—Marsala, for example, where the sands of the African deserts directly arrive?'

Thus in Rome it was held that malaria was transported on the wings of the *scirocco* from the Pontine Marshes.[1] Lancisi was the authoritative supporter of this theory, which vanishes directly one considers that between the Pontine Marshes and Rome are interposed the Latial Mountains, including Monte Cavo, which are delightful places, that are never infested by malaria; while if the theory were true they would be malarious in the highest degree. Consequently, Baccelli justly maintains that all the Pontine Marshes could not be charged with a single case of fever which occurred within the walls of Rome.

And in fact the *scirocco* that comes from Africa and passes over these marshes cannot beat directly on Rome; but there is also another wind, the *libeccio* (south-west wind), which, however, no one has ever thought of charging with this hypothetical transportation of malaria.

In Rome it was likewise believed that malaria was carried thither from the marshes of Ostia and Maccarese, and therefore by the west wind, that is, by the sea breeze, which traverses the Roman Campagna. And in consequence of this hypothesis they deemed it urgent to drain these marshes, and proceeded to hurried works of sanitation without thinking how strange it was to incriminate that wind with malaria which, freshly blowing in the summer afternoons, renders Rome one of the most delightful cities in Italy, even in the hot season.

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[1] This disease now never, or hardly ever, occurs within the walls of Rome in any season of the year.—[TRANSLATOR.]

The wind, therefore, cannot transport malaria: on the contrary, it acts on the malarial virus, as on other virus, clearing and dispersing the pathogenic germs in the atmosphere. Analogously we know that the fragile mosquitoes do not resist the wind, and when this blows they do not come out from their diurnal hiding-places, nor do they attack man, even at sunset. Our rustics know well that in the evenings in which the wind blows they can sit outside their habitations without being molested by the bites of mosquitoes.

It is possible, however, that light winds may sometimes cause the diffusion of mosquitoes. Ficalbi admits it, but the subject requires further study.

A direct outcome of the above-mentioned wind-borne theory of malaria was another which claimed that *woods* filtered the malarial germs in such a way that a wind passing through a wood came out purified of them. The celebrated Lancisi was also the supporter of this theory, which he maintained with great ardour *à propos* of the disforesting of the woods near Cisterna (fig. 25).

This town and the surrounding territory belonged for a very long time to the Caetani family, which in 1714 was much in debt, and consequently thought of gaining a large sum of money by ceding to a Tuscan contractor the right of cutting down the woods about Cisterna. Having applied for permission to Clement XI., Lancisi arose to combat this destruction as dangerous to the public health of Rome, and on the occasion he delivered two memorable discourses before the Congregation of Health to demonstrate that those woods retained the noxious effluvia of the Pontine Marshes. 'Even the ancients,' said Lancisi, 'knew well how much the woods were the true guardians of health, and therefore they put them under the protection of the gods.' And he added that the woods filtered the low winds; and these are precisely the hot *scirocco* winds which arise from on high and come on the continent to sweep the ground; while the cold winds arise from below, and, as they gradually disperse from their place of origin, gain a higher level in the atmospheric strata.

This opinion is, in truth, contrary enough to the principles of physics. Really the hotter winds, and consequently the lighter, sweep the ground! And even if it were so, how could the thickest foliage of the tallest trees filter such a high aërial current?

As regards the testimony of the ancients, we must remember that, according to Di Tucci, their worship of trees was confined to the *sacri luci*, the *sacra nemora*, and the *sacra robura*, which grew around the temples, or protected the altars dedicated to special religions and to particular sacrifices. This is so true that woods were also consecrated in very healthy localities.

In conclusion, we can formulate the following principal axioms regarding the propagation of malaria by the atmosphere :—

1. The hours during which the malarial germs are most plentiful in the air are those of the evening, sunset, and night.

2. They generally rise from limited foci, and are diffused to a limited distance in the horizontal, oblique, and vertical directions.

3. The winds, properly called, do not generally transport them, they tend rather to diminish their number in the atmosphere.

4. Woods, instead of filtering them, may be foci of malarial infection.

These axioms are thoroughly in accordance with the theory that the malarial germ is cultivated, transported, and inoculated by the agency of mosquitoes, which—

1. By day live hidden and sheltered, while they come out to bite man in the evening and night.

2. They do not wander far from the place where they are born, and especially they fly a little distance from the ground.

3. When the wind blows they do not, as a rule, come out of their hiding-places.

4. Shady and damp woods and trees in general are the nests of mosquitoes.

The mosquito, besides being the source, is consequently also the carrier of malarial infection.

Of the *connection between malaria and mosquitoes* indications are found even in ancient authors, such as Columella and Varro, and *popular experience* has admitted it for a long time. One not rarely hears these words from the mouth of the peasants of the Agro Romano: 'In such a place there is much fever, because it is full of mosquitoes.' And there are a few customs which have been unconsciously inspired by this idea. For example, when the shepherds return from the Apennines, where they have passed the summer, to their cabins in the Roman Campagna, generally in the months of September and October, they do not occupy them before thoroughly smoking them to drive out the numerous mosquitoes; and frequently they make the sheep sleep there for some days, with whose blood the famished mosquitoes satiate themselves.

In Eastern Africa malaria and the mosquito are called by the same name, *Mbù*.

In *medical literature*, also, this opinion is ancient. Evidently Lancisi expounds and maintains it, who (*loc. cit.*) after having demonstrated that *minima insecta* (that is, as we say, *Culicum ingens copia*) *paludibus innasci, atque sub organicorum effluviorum forma per circumfusum aerem dispergi*. In the same book, cap. xviii., he maintains that, these *venenata animalia non occidunt vulnere, sed infuso per vulnus venefico liquido;* and he also expresses the doubt whether these *insecta dum cutem morsu sauciant ova sua deponunt*, and finally maintains that these *palustria insecta noxium succum infun-*

dunt, and suspected that the said *vermes sanguineis vasis sese inferant!*

In America, where also this intimate connection between malaria and mosquito is commonly recognised, Nott, so long ago as 1848, maintained that yellow fever was transported by means of the mosquito, and he supposed the same for malaria.

Here among us Angelo Alessandrini, towards 1870, in an agrarian and hygienic study on Rome and Latium, wrote that the mosquito, 'with the vehicle of the unhealthy air from the open country, passes into inhabited places, invades the habitations, hides itself during the day to hum in the night in search of man in repose, . . . and, by means of its bite, inoculates its poison.'

Another American physician, King, putting together the facts gathered from popular tradition with the facts revealed by epidemiology, maintained, in 1883, that malaria is transported by the agency of mosquitoes.

In 1884 Laveran, by analogy with the already cited studies of Manson, asked the question: 'Do mosquitoes take a part in the pathogenesis of paludism as in that of filariasis?' The thing, he adds, is not impossible; and it is to be noted that mosquitoes abound in all marshy localities.

In Flügge's treatise on hygiene, even in the first edition (1889), it is stated that malaria might be transmitted by insects as well as by the usual vehicles (air, water).

In 1891 Laveran modified, after the publication of my researches, of which we shall speak presently, his old opinion favourable to the hypothesis of water as a vehicle of malaria, in the sense that the specific germs, with the mosquitoes which die, are transported in the water, and man, drinking this water, becomes infected, analogously to that which Manson had maintained for filariasis.

The mosquito hypothesis was also mentioned in 1892 by R. Pfeiffer and by Koch, who lately has again maintained it.

In 1893 Smith and Kilborne made their discovery, already mentioned, of the transmission of bovine malaria by means of ticks.

Manson, in 1896, and in the same year Laveran also, insisted on the analogies of propagation, according to them, and according to what we have said already (see page 62), of malaria with filariasis.

Bignami, who, in 1894, together with Dionisi, had endeavoured experimentally to demonstrate the mosquito hypothesis, in 1896, in an article in reply to Manson, combated with my arguments the water hypothesis; he demonstrated that the hypothesis of the mosquitoes explains very well the epidemiological data of malaria, gave the proof that it is sufficient to inoculate a very minute quantity of blood—that which remains adherent to the fine needle of a Pravaz syringe—to reproduce malaria. Analogously also the mosquito would be able to carry the infection from one man to another; and he concluded that malaria bears itself in respect to man as if it had been inoculated by mosquitoes.

In the same year (1896) Mendini, in his 'Guida Igienica di Roma,'[1] supported the hypothesis of the inoculation of malaria by mosquitoes; and in 1897 Coronado of Havana gave great importance to these arthropoda in the propagation of malaria.

Up to then, however, only indirect arguments were forthcoming. The direct experimental proof was given only recently with the above-mentioned studies of Ross on the malaria of birds, and with the studies made in the Santo Spirito Hospital by Grassi, Bastianelli, and Bignami on the malaria of man.

For some time Bignami caused healthy men to be bitten by mosquitoes captured in malarious places; these were afterwards found to be of the genus *Culex*. But he did not succeed in reproducing the fever. Then came Grassi, who suggested using the *Anopheles*, and by their agency malarial fever of the æstivo-autumnal type was experimentally reproduced for the first time in man, and subsequently the spring tertian was also reproduced by the same means.

The objection that these experiments prove nothing in a positive way, inasmuch as at Rome, and in the Santo Spirito Hospital, malaria could be contracted spontaneously, falls to the ground before the mildest criticism. The experiments have always been made on persons who for years have been under medical supervision in the Hospital, that is, in a place immune from malaria.

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[1] This book has been translated and edited by me, with the title of Dr. Mendini's *Hygienic Guide to Rome*. (The Scientific Press, London, 1897.)—[TRANSLATOR.]

Moreover, there are now many cases of the reproduction of malaria in man by the bite of special infected mosquitoes. And, therefore, *up to now, of all the supposed vehicles of malaria, this of the mosquitoes is the only one that has been directly and undoubtedly demonstrated.*

But is there not some other vehicle of malarial infection than that of mosquitoes?

We have already recorded our experiments, from which it resulted that in birds we did not succeed in reproducing their malarial infection by the inoculation of the earth of even intensely malarious spots.

Consequently, if up till to-day it has not been demonstrated that the malarial germ exists directly in the ground, one certainly cannot admit that a person can breathe it with the dust which is raised from the ground.

The hypothesis of **water** as a vehicle for malarial infection remains to be considered.

Even since the latest researches have been published, the doubt has been revived, as we have said, whether, besides the two life-cycles of the parasites already described, there is not at the end of the sexual cycle a resisting spore stage, by which the parasite resists the influences of the external world, and more especially when in water, for a variable time, independently of its life in the mosquito's body. We have said that the morphological and experimental studies have not, at least up to now, confirmed this hypothesis of resisting spores, which, nevertheless, may exist; and therefore it is necessary to discuss whether the water, that may eventually contain them, can also when ingested infect man.

That marshy water when drunk produces malaria is universally believed in by the people who live in malarious places. But here popular experience loses all its value when one thinks for a moment that these persons, who believe that they drink the germs of malaria, are living at the same time in bad air.

Even Hippocrates wrote that he who drinks, in the summer, the warm and fœtid stagnant water of marshes acquires from it an enlarged spleen, a hard belly, and the water accumulates under his skin: in short it may even produce malarial cachexia.

This judgment was accepted in the medical schools until J. M. Lancisi, with his great authority, caused the idea to prevail that stagnant waters produced malaria by their noxious effluvia and not by drinking them.

Lancisi's opinion was almost universally accepted in 1848, when Boudin, one of the most esteemed French epidemiologists, described minutely a ship epidemic, the celebrated epidemic, according to him, of malaria on board the no less celebrated ship, the *Argo*.

As this epidemy is constantly brought forth as a triumphant proof by those who believe in this hypothesis of water infection, it is advisable to speak of it somewhat in detail, to see whether, when judged by sound criticism, one must not arrive at an opposite conclusion.

Towards the middle of July 1834, 800 French soldiers were embarked at Bona, in Algeria, for Marseilles.

These soldiers were conveyed in three ships, 120 of whom were on board the transport ship *Argo*. While those on board the other two ships had an excellent passage, on the *Argo*, soon after its departure, a terrible epidemy broke out. It was believed to be a very severe malarial infection, from which thirteen died during the passage, and ninety-eight landed at Marseilles with symptoms of choleraic, epileptic, tetanic, comatose pernicious fevers, which yielded as if by enchantment to the use of sulphate of quinine in large doses.

As the *Argo*, in the hurry of departure, had shipped for drinking purposes the impure water of a pond near the port, and the soldiers had drunk freely of it, it was universally said that the water was the cause of this very severe epidemy.

But the voyage between Bona and Marseilles is short, and it is strange that a malarial infection should have arisen so suddenly, without the period of incubation which is always observed.

It is also strange that all were taken ill, and that in all were suddenly manifested those terrible forms of pernicious fever, many of which were fatal. Even in districts of very severe malaria, a group of persons going thither are not certainly all taken ill immediately and contemporaneously; much less do they suffer from pernicious fever on the first day of the disease. The very severe forms of malaria become pernicious during the second or third attacks, but they are never such at the first attack.

The principal argument brought forward by Boudin was that the above forms yielded like enchantment to quinine.

But are the pernicious malarial fevers cured in the proportion of $^{100}/_{100}$, even when treated with very large doses of quinine? And even when the gravity of the infection is overcome by this invaluable drug, do not they usually recur for months and months?

It is evident, therefore, that the above outbreak was not due to a malarial infection, but rather to an acute poisoning from which many died; and the greater number were cured after some days, but certainly not by the quinine given them.

There are other examples in medical literature of ship epidemics of malaria which were said to have been caused by drinking infected waters, but they are cited in such an uncertain and frequently erroneous way that they do not merit scientific discussion. Up till now, therefore, no one has been able to adduce an undeniable example of the transmission of malaria by means of the water of malarious places. Yet it has been maintained that malaria is synonymous with *malacqua!*

Epidemiology, on the contrary, demonstrates by numerous examples that people who in malarious districts drink excellent water are not proof against malaria; and, *vice versa*, experimentation has demonstrated that persons who in very healthy localities drink the marshy waters of malarious districts never take malaria.

From the bottoms of the hills and mountains which surround the Pontine Marshes (fig. 25) an enormous quantity of water is discharged, which gathers immediately at the sources into true rivers which, having to traverse a vast plain with very little fall to the level of the sea, produce these enormous marshes. This pure water is freely used by the people who live near the hills, where, notwithstanding, malaria reigns in all its virulence.

The town of Sermoneta, which has been almost destroyed, as we have said, by fevers, after the badly executed reclaiming of the Pontine Marshes, thought of saving itself by conducting into the town good potable water, but nevertheless the mortality was not lessened; and if recently the town is more healthy it is due to the rational works of sanitation in the underlying plain.

Along the Rome-Tivoli railway, one of those which, in Latium, enjoy the sad *primato* of malaria, to every railway cottage has been brought, by special pipes, a constant supply of the Acqua Marcia, with the hope that with such a splendid water the fevers would disappear. But instead, during the summer of 1898, of the railway *personnel* all fell ill except three, who remained immune, as we shall see, in consequence of their special individual resistance.

Experiments have also been carried out on a large scale, by making men, living in healthy places, ingest water from malarial centres. These experiments were initiated by me, with the feeling that while it was very important to solve a problem of such high human interest, on the other hand, it had been known for a long time that decaying materials are innocuous when introduced into the stomach of man or of the lower animals; and that if malaria subsequently developed through drinking these waters, by making the diagnosis immediately by the examination of the blood, and administering the specific remedy directly the first attack appeared, no harm would ensue.

The marshy water was administered by ingestion, inhalation, and enteroclysm. On the next page we give a table of all the experiments of the kind made during recent years, from those which I conducted in 1886 until the present time.

More than sixty persons were subjected by various authors to the ingestion of marshy water. The quantity of water drunk was large, up to 2–3 litres a day, and it was taken from intensely malarious places, and always in the summer and autumn months. All the experiments, from mine to those of Brancaleone, Zeri, Salomone Marino, demonstrate that the fever is not taken by the ingestion of marshy water.

It may be objected that the malarial germs,

TABLE V.—DRINKING-WATER AND MALARIA.

	Number of persons experimented upon	Duration of the experiments	Daily quantity of water per individual	Place from where the water came
(A) Ingestion	6	Days 8-15	300-3,000 c.c.	Pontine Marshes. Ponds of the Agro Romano.
	12	12-21	1,000-2,000 c.c.	Valguarnera in Sicily.
	30	5-20	2,000-3,000 c.c.	Tuscan Maremma. Agro Romano.
	25	6–24	In total, 5·24 litres	Vallomonica. &c., in Sicily.
(B) Inhalation	16	2–15 Twice a day; 20-30 minutes' duration	Total, 157 litres	Pontine Marshes. Cervara.
(C) Enteroclysm	5	2–14 Two enteroclysms per day	Total, 64 litres	Pontine Marshes. Cervara.

introduced with the water, were destroyed in the stomach. This is not very probable, inasmuch as the barrier of the stomach is not very potent even against truly intestinal infections, such as cholera and typhoid fever.

But malaria may act differently. Then I thought of introducing the water by inhalation and by enteroclysm; but even by these paths Dr. Zeri never succeeded in reproducing the mildest fever.

Therefore *water is not the vehicle of malarial infection: the epidemiological data prove it; a long series of experiments confirm it.*

And what other vehicles of malaria may there be? One may suspect vegetable alimentary substances.

Even in plants endocellular amœboid parasites are known; it is sufficient to mention the famous *Plasmodiophora Brassicæ* of Woronin, which in 1885 was then, for us, the best example of analogy for maintaining the parasitic nature of those endoglobular bodies that, by analogy, Marchiafava and I called plasmodia of malaria.

But of this last hypothetic vehicle it is not now necessary to speak.

After having passed in review all the possible vehicles of this epidemy, we can conclude that *up to now the certain vehicle, and at the same time the certain source of the malarial infection, are special mosquitoes, and the air is the vehicle of malaria, inasmuch as it is the vehicle of the malarial mosquitoes.*

PATH OF PENETRATION OF THE MALARIAL GERMS INTO THE ORGANISM

The most undeniable is *the skin*, bitten by the proboscis through which the infected mosquito inoculates its sporozoites. A single mosquito in one or more nights can bite and infect many persons. How this happens is demonstrated by fig. 26, after Ficalbi, which gives us a clear idea of the biting apparatus of the *Culex pipiens.*

This apparatus is hidden within a sheath (1), terminating in an olive (2), and consists of six pieces: the lip (3), the epipharynx (4), two mandibles (5), and two maxillæ (6). The lip terminates in a sharp oblique point; the two maxillæ terminate in a serrated extremity. When the mosquito bites, the sheath does not penetrate the skin, but bends toward the thorax, and the stylets contained in it pierce the integument; these are capable of penetrating even a very hard skin like that of the ox, or of biting through clothes if not very thick.

The sporozoites having filled, as we have already said, the tubules of the salivary glands, one understands how they are inoculated with the saliva during the act of biting.

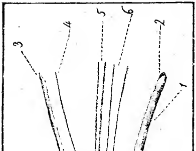

FIG. 26.

There is nothing to support the idea that the germs may enter by way of the *stomach*; and after the latest studies the *respiratory path* is to be rejected, at least so long as resisting spores of the hæmosporidia are not demonstrated free in the environment. Up till now malarial germs have not been found directly in the earth; it is difficult therefore to imagine how they can be contained in the dust which is raised from it. And besides, in the cases of autopsies of those dead of pernicious fever, Bignami has never been able to discover in the peribronchial glands anything resembling a malarial germ.

Consequently *the skin is the only certain path of entrance that now remains.* But as long ago as 1853, Marmocchi, in his 'Universal Geography,' wrote: 'As the marsh-miasma insinuates itself into our bodies to infect them, . . . on the guidance of simple logic it appears very probable that the poison is inoculated in the human body not by the paths of the respiration, but through the pores of the skin.' And this path is more than sufficient; the germs immediately gain excess to the circulating blood, and here enter the red corpuscle and multiply in it, passing through their asexual cycle of life, and preparing the gametes for the preservation of the species external to man.

It is remarkable that the *Anopheles* mosquitoes, which are undoubtedly injurious, do not when flying make a humming sound, and that their bites are less irritating than those of the *Culex*. Very frequently persons living in the Campagna are not aware that they have been bitten by them.

CAUSES OF PREDISPOSITION OR OF IMMUNITY.

No epidemy can be thoroughly understood if we do not recognise the enormous importance of the indirect epidemic causes, which predispose to or immunise against the development of an epidemic disease. One cannot, and should not, act differently when considering the epidemiology of malaria.

These very complex causes we divide, as they always are divided, into organic or individual, local or physical, and social.

We begin with the

ORGANIC CAUSES OF PREDISPOSITION OR OF IMMUNITY.

It is universally admitted that the *chilling of the body* is a cause of predisposition to malaria. Horace even speaks of it when he describes the mother who dipped her child in the waters of the Tiber to appease the goddess Fever, and quickly the baby is seized with 'frigid quartan.' And Doni said that in the Campagna *noctes æstate nimium frigidæ insalubres.* Indeed, the well-to-do inhabitants of the Agro Romano are so well aware of this fact that, in the early morning, evening, and night they always wear, even in the summer, their winter greatcoats, dreading the fall in the temperature. The chilling of the body easily occurs here, where in a single day there are notable changes of temperature. And it is for this reason that in Rome, during the summer, the evenings, nights, and still more the early mornings, are always very fresh; and inasmuch as the maximum temperature occurs about midday, in the short space of a few hours, as we shall see later on, there are very great thermic oscillations.

Baglivi has written that: *estate sudore madere et aurem frigidum accipere pestis est.*

In the beginning of the century (1803) Morichini believed that the difference between the temperature of the days and nights in the summer disposed to malarial diseases.

Later on Santarelli (1808) and Folchi (1845) maintained positively that the humidity and cold of the nights were the undoubted cause of malarial fevers, because they suppressed the perspiration.

Nevertheless, following Brocchi (1820), Minzi recognised (1844) that chilling by itself alone was not the cause of fevers. 'It is not impossible,' he added, 'that a specific modifier, . . . unknown to the senses and not recognisable by physical and chemical means, exists in the atmosphere of marshes, and is the element indispensable for intermittent fevers; but daily observation proves that it remains completely inactive if particular circumstances do not concur in promoting its morbid efficacy.'

Chilling of the body is a predisposing cause both to the onset of the primary infections and also to the succession of the malarial recurrences. Indeed, a febrile attack has been several times observed to supervene after a cold bath, in persons liable to malarial paroxysms.

Recently also Oldham (1871) and Baker (1888) have supported the hypothesis of chilling as a cause of malarial fevers. According to this latter author the presence of intermittent fevers in all parts of the world is proportionate to the difference in temperature between the day and night, that is, to its mean diurnal oscillation. This relation was observed month by month, in 542,009 cases of fever, during the years of the American War, from 1861 to 1865.

The predisposing effect of chill is well seen in the Campagna. At harvest time, the poor labourers, badly clothed, insufficiently fed, and bathed with sweat, in order to obtain a little relief for their weary limbs, expose themselves to the cool breezes, and at night sleep in the open air. In such cases we can well conceive how the individual, who carries malarial infection in its latent form, suffers from fever which is the active manifestation of the infection, as soon as his vital powers are lowered by these depressing influences. It is well known how they dread being attacked by fever when a heavy shower falls.

Consequently *it is very probable that the chilling of the body is an organic cause predisposing to malarial infection.*

Does the predisposition to malaria vary according to age?

Our statistics of the causes of death in 1890 give the following percentage mortality :—

TABLE VI.—MORTALITY OF MALARIA ACCORDING TO AGE.

From birth to 5 years	From 5 to 10 years	From 10 to 20 years	From 20 to 40 years	From 40 to 60 years	From 60 to 80 years
19·4	48·9	38·6	24·3	23·9	23·9

Therefore no age is spared—furthermore, it is very certain that children are most frequently attacked, and in them malaria is very prevalent; but the above statistics enable us only to affirm that the highest mortality from malaria occurs between five and twenty years of age. Exact data as to the morbidity and mortality of children from this disease are still wanting.

Does *an immunity* from malaria exist? We shall first consider congenital, natural, or race immunity; secondly, acquired immunity, and finally artificial immunity.

Natural immunity.—Are there races immune from malaria?

Comparative epidemiology proves that in the lower animals there are immune races. For example, bovine malaria rarely attacks the indigenous oxen of the Agro Romano, while it decimates those imported from Holland, Switzerland, Lombardy, &c. A few years ago, here at Tor di Quinto, they tried to institute a large dairy farm, and about one hundred Dutch cows were imported into that malarious district; a very severe epidemic of malaria destroyed the whole herd, one solitary cow surviving! I have studied and described similar outbreaks near Rome, for instance, at Cervelletta, and Bocca di Leone.

But among the human races are there some refractory to malaria?

Some colonial medical practitioners have been able to study contemporaneously the behaviour of two or more human races in a malarious locality. A valuable work of the kind is that of Maurel. From his studies it results that practically *no human race is immune* from malaria, not even the black race, which by some are believed to be immune. In places where severe malaria exists, certainly the black population which inhabits them acquires a relative immunity to the disease; but if in these same places another black population arrives which previously inhabited non-malarious places, it is decimated by the fevers.

A white population also, which for centuries has lived in regions of intense malaria, finally acquires a relative immunity against malaria, that is, adapts itself to resist it.

Especially when the action of an heroic drug, such as quinine, has not intervened, the part of the population which in malarious places has survived is that specifically more resistent; and thus gradually, from generation to generation, the Darwinian law of natural selection, which has been so well illustrated in this case by Tommasi-Crudeli, has produced a race continuously more resistent against this infection.

By this means a remarkable population, whose ancestors have lived in the Pontine Marshes for centuries, has become resistent to malaria; while a colony of Venetians, who were lately brought thither, were literally decimated by the fevers, and the survivors fled in terror. It is not that the inhabitants of the place do not pay their tribute to the goddess Fever, but certainly they live in sites where other populations would be exterminated. So also at Ostia there is a colony of agricultural *romagnoli* who, not being hereditarily protected against malaria. suffer much from the disease, and unfortunately often die of it, notwithstanding that they live in fairly good hygienic conditions; while, on the contrary, in that same region live also the so-called *capannari* (hut-dwellers), who for centuries have descended from the mountains into the Agro Romano and remain there for many months in the year; and though they live, as we shall see, in huts, have insufficient food and clothing, still they suffer from malaria to a much less extent than do the *romagnoli*.

Therefore the fact of a natural relative immunity of some races against malarial infection is evident.

How does this relative immunity come about? For the most part it is undoubtedly due to those acquired habits, especially in relation to habitation and work, which experience has taught are the most efficacious for preserving oneself from the fevers.

There are also individuals immune in the most absolute degree by organic causes peculiar to themselves. For example, at Sezze, in the Pontine Marshes, we have obtained the precise histories of four individuals who are absolutely immune from malaria, notwithstanding that they have lived there for years without taking the least precautions—they work very laboriously, have insufficient and bad food, frequently sleep on the marshes, in the open air, and in such a manner as to be continually bitten by mosquitoes; still they have never had malaria, are very healthy, have a rosy colour, and their liver and spleen are normal in size.

I have met with similar fortunate individuals also in other intensely malarious regions.

It is difficult to say what the mechanism of this organic immunity is; certainly it cannot be explained by the hypothesis of antitoxins in the serum. In fact, we have bled the above-mentioned individuals, have taken the serum of their blood and inoculated it in a man, and then injected into him the malarial blood of mild or spring fevers. The preventive inoculation of this serum did not in the least prolong the incubation period of the fever. So that it is little probable that those individuals are immune because they have immunising principles in the serum of their blood.

We shall now see what at present is known concerning *immunity acquired by malarial infection.*

This infection easily recurs; he who has already suffered from it, as is generally known, is more predisposed than others to new infections. Consequently, as a rule, the opposite to a consecutive immunity is verified.

But I have collected well-ascertained cases of persons who have reached malarial cachexia, with extreme anæmia, with enormous enlargement of the spleen and liver, and then I have seen the spleen and liver very gradually become reduced to their normal limits, and in these persons a species of natural immunity has afterwards remained. A typical example of this kind I have met with on the Rome-Civita Vecchia line in a railway man who, after having suffered for a long time from malarial fevers going on to cachexia, subsequently regained his health. For many years he has lived safely in the midst of the destruction of his family, and he is the sole survivor of his companions who came with him to work on that line. I have met with three other typical examples on the Rome-Tivoli railway.

One of these three, having been brought almost to death's door by malarial cachexia, went to the mountains to regain his health, was cured there, and then returned to his work; and he has not since been attacked by fever, not even in the year 1898, when all the members of his family were stricken with the disease.

This occurrence is, however, rather rare; in fact, as far as I know, it is the first time that it has attracted the attention of students of malaria. This immunity is not so stable as that of congenital origin; for example, one of the three who after grave cachexia had been immune for ten years, in 1898 was taken ill with fever, from which, however, he was quickly cured. In other cases also I have seen the febrile infection run a very mild course in those persons who enjoy a relative immunity following a recovery from malarial cachexia.

In cases still more rare one may acquire an immunity after a mild and short attack of malaria, which has been cured with quinine.

Consequently an immunity following malarial infection exists, but it is not generally so persistent as a congenital immunity.

Can we obtain an *artificial immunity?* This is a problem of the greatest interest. If we could confer immunity by artificial means, one of the gravest human problems would be solved.

We have made many attempts, guided by the various theories which are held regarding immunity. Starting with the idea that in an acute malarial infection a toxin is produced as in other infections, we have thought, that if a toxin develop in the rigor stage and during the fever, an antitoxin must also be produced in the stage of defervescence. I have therefore bled fever patients during defervescence, I have put together the serums, and tested them to see if they possessed immunising and therapeutic properties. Moreover, if these antitoxins exist, they must be produced in large quantity, even in cases of spontaneous cure. Well, I have also experimented with the serum of these cases thus cured; but in neither instance have we obtained any immunising result.

Consequently, for the present we must maintain that just as we cannot demonstrate (see p. 56) a malarial pyrogenic toxin, neither can we demonstrate a relative antitoxin. The one fact is the consequence of the other.

We have also experimented with the blood serum of animals congenitally immune against malaria, such as, for instance, the oxen of the Agro Romano; but even here we obtained no positive result, or perhaps only a lengthening of the incubation period of the malarial infection experimentally produced with the introduction of malarial blood after the inoculation of the supposed immunising serum.

Acting on the idea that the antitoxins in infective diseases collect and concentrate especially in certain organs, we have made attempts at *preventive opotherapy*, utilising the organs of animals typically immune, that is to say, the buffalos and oxen of the Agro Romano. We have experimented with the juice of the following organs: brain, lymphatic glands, spleen, bone-marrow, liver, and pancreas. These organs were pounded up with sterile sand, and then subjected to the high pressure of 500–600 atmospheres in a hydraulic press. First the blood was expressed, then the intercellular plasma; the final pressure yielded the true cellular juice, which was inoculated. But neither the preventive nor the curative opotherapy had any effect. The same can be said of the preventive inoculations of large quantities of blood of bovine malaria, and of the serum of the blood of the same cattle cured of their malaria.

We also wished to ascertain if there were any antagonistic substances in the *Culex*, and if so, whether they checked the growth of the hæmosporidia of human malaria, and also if they existed in the non-infected *Anopheles*, or developed only in those who were infected. In the hope that these substances were present and that an artificial immunity might thus be transmitted to man, we prepared, with the most scrupulous antiseptic precautions and repeated filtrations, the juice of many of the above-mentioned mosquitoes, and we inoculated it freely and repeatedly into three persons, without, however, being able to prevent in them the development of experimental æstivo-autumnal malaria, which had been produced by the inoculation of half a gramme of malarial blood.

We likewise experimented with medicinal substances. The immunising action of quinine has been much discussed, and some authors admit it; certainly, however, it is not of practical use, inasmuch as it is a remedy which in small doses is inefficacious, and in large doses cannot be taken for a long time, as it is injurious to the digestive and nervous systems. It consequently has not had, and never can have, extensive application, whatever Koch may think of it.

We have, however, tried to adapt one horse, and then another, to progressively increasing doses of quinine, administered by the mouth, subcutaneously, into the trachea, and into the veins.

The horse having reached a tolerance of 20 grammes given in one dose intravenously, we extracted the blood and prepared a serum which proved, even in large doses, to be inefficacious both as a preventive of experimental malaria and as a curative of the natural infection.

We then tried other remedies which can be taken for a long time, even in large doses; such as *potassium bromide*, *potassium iodide*, *arsenic*, *carbolic acid* by subcutaneous injection; *antipyrin*, *phenocoll*, *methylene blue*, and *euchinin*, a preparation that has an anti-malarial action analogous to that of quinine, but without producing all the disturbances, and without possessing the disagreeable taste of the latter drug.

Of these preparations used as immunising substances against experimental spring malarial infection (mild tertian and quartan), the iodide and antipyrin had negative results; the bromide, phenocoll, and arsenic yielded once a positive result, and on another occasion a negative one; the carbolic acid once a doubtful result; the euchinin and methylene blue twice positive results. The last two drugs immunised man from inoculations of from one to two grammes of æstivo-autumnal blood. We ought therefore to experiment with them on a large scale, as immunising against the natural malarial infection. Euchinin, however, is still too dear, and also produces some of the disturbances of quinine. Methylene blue is perhaps more practical. At any rate it has been proved that *by means of medicinal substances an immunity even against the most severe experimental malaria can be produced in man.*

In some cases in which we have had, as I have said, negative results, the incubation period was prolonged. Nevertheless, these experiments strengthen our opinion that the incubation period in experimental malaria is very much longer than has been generally stated by authors. The periods of its maximum duration, according to Bignami and Bastianelli, are as follows:—

Quartan, 15 days.
Spring tertian, 12 days.
Æstivo-autumnal tertian, 5 days.

We however have seen the incubation period in the case of quartan infection to be as long as 47 days without any drug having been given, and in one subject who had been treated with phenocoll 66 days.

In the spring tertian we have observed an incubation of 22 days; in the æstivo-autumnal tertian, 17 days.

Therefore the incubation period of artificial infection may be very long; and thus perhaps are explained the long-interval recurrent fevers.

The prolongation of the incubation period depends more on the greater specific organic resistance than on the efficacy of remedies. That there are persons endowed with this greater resistance there is no doubt. In an individual who never had suffered from malaria, and did not live in malarious regions, the injections made with a considerable quantity of blood of spring tertian and then of æstivo-autumnal tertian were completely negative.

The problem of artificial immunity against malaria is consequently still an *incognita*, to solve which it is necessary to work on other lines. Nevertheless, we have a sold basis to start upon. That is, *there are individuals immune not only from natural but also from experimental malaria.* Studying the mechanism of the immunity of these individuals, perhaps one will be able to transmit it to others, solving a problem of the greatest hygienic and economic importance. Up to now the only successful attempts at artificial immunity are those obtained by the above-mentioned drugs.

LOCAL OR PHYSICAL CAUSES OF PREDISPOSITION OR OF IMMUNITY.

These factors also have enormous importance in relation to the production of malaria. Up till a few months ago this was believed to be one of the most typical soil diseases, like tetanus and anthrax. This can no longer be maintained *sic et simpliciter*; but, on the other hand, it is undoubtedly, as we have said, a typical local or autochthonic epidemy. It is interesting, therefore, to study the local causes which favour or do not favour its production.

In studying these causes we shall divide them, with Pettenkofer, into conditions of place and conditions of time.

CONDITIONS OF PLACE.

It is necessary, above all, to examine the three principal factors; that is, the *soil*, the *water*, and the *air*.

Soil.—Malarious soils are found all over the surface of the globe, with the exception of those situated beyond the polar circles; there is no quality of soil which can be said to be *a priori* incapable of favouring the development of malaria.

Even on madreporic soils, and also on granitic soils, the development of malaria has been observed. Tommasi-Crudeli has stated that malaria arises on soils of the most varied composition and situated in every kind of position, both volcanic and sedimentary, of all geological periods, and even in soils of quartziferous sand without vegetation. In the Roman Campagna there are on the surface of the ground no less than thirty-five varieties of soil, and there is reason to believe that not one of these is incapable of favouring the development of malaria.

It is not, therefore, the soil *per se* which influences the production of malaria, but only to the extent that it retains water on its surface. Some soils readily permit the water to percolate through them, and consequently marshes are never formed. Other soils, on the contrary, are only slightly permeable, and stagnant waters readily collect on their surface.

It is necessary, therefore, to take into consideration all those properties of the soil which have an influence on the water it contains. It is known that the capacity of a soil to retain water, and its capillary power of absorbing water, and perhaps also its power of condensing the humidity of the air, act in one direction: the faculty of the soil of allowing water to pass through it, that is its power of filtration and its power of evaporation, acts in the opposite direction.

These are the regulating forces that influence the ground-water which has so much importance in the local production of malaria when it remains on the surface. One understands, consequently, how all the conditions of the soil that cause it to remain on the surface must also have great importance; thus, for example, fractures in volcanic ground, the erosions produced by water flowing along valleys, and broken country form channels through which the ground-water wells up to the surface.

The Roman *Campagna*, with its undulations, valleys, and its innumerable perennial streams and torrents, is a typical example of what we have described, and therefore, also, a typical focus of malaria.

Consequently, for a soil to be favourable to the development of malaria it is necessary that water remain on its surface. The amount of water may be very small, as Tommasi-Crudeli has justly maintained; but it must last at least during the period of the larval stage of the malarial mosquitoes. If after this period the soil for a certain time become dry, malaria may still persist, because adult mosquitoes do not require water.

Water.—*Water is necessary to the development of malaria, inasmuch as it is necessary to the life of the larvæ of the malarial mosquitoes.*

From Lancisi's time onwards only extensive *marshes* and large *ponds* have been considered the focus for the development of malaria, and great importance has been attributed to the *putrefaction* of these waters, and to the effluvia they develop. Then arose the Tuscan medical school, which proclaimed the necessity of *mixture of fresh with salt water*.

We shall examine briefly the bearing of these hypotheses.

The total surface of the marshes of Italy, according to the calculations made in 1885 by Pareto, amounted to 1,098,961 hectares. More recent calculations give the total surface of Italy as 28,658,900 hectares, of which the ponds and marshes occupy 1,287,372. If, on the other hand, we remember (see fig. 3) the extent of Italian territory invaded by malaria, the disproportion between this epidemy and paludism becomes evident, admitting also that malaria extends for a certain radius around each marsh. Here in the Agro Romano, states Tommasi-Crudeli, if malaria were connected solely with the marshes indicated in the geographical maps (and in part now reclaimed by drainage works), it would, in truth, not be very extensive. Furthermore, it is known that there are many marshes without malaria, even with the favourable conditions of temperature, especially in the other hemisphere. And now Ficalbi rightly distinguishes the paludal mosquitoes from the malarial mosquitoes. The latter are the *Anopheles*, and the former are various species of *Culex* (*penicillaris*, &c.) Therefore, all paludal mosquitoes are not malarial.

And neither can it be maintained that stagnant waters must be putrid to generate the miasmata of fever. Minzi, Colin, Tommasi-Crudeli have demonstrated the fallacy of this opinion; and recent researches prove that the malarial mosquitoes do not generally deposit their eggs in putrid waters, and consequently their larvæ are not found in them, and that if they are placed there they quickly die.

Then admixture of sea with fresh water

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occurs in many parts of the littoral where the coast is very low, so that when the sea rises the discharge of the fresh waters into it is obstructed, and swamps and marshes are formed, frequently with the putrefaction of the plants or animals which habitually live only in one or other of the mixed waters. This stagnation may constitute a condition not altogether unfavourable to the development of malaria, inasmuch as a certain quantity of sodium chloride and of the products of putrefaction is not, as we have said, hostile to the life of mosquitoes; but certainly it is not a condition necessary to the production of malaria, because the places infested by this pestilence are not unfortunately confined to the coasts, but extend into the centre of the continents.

Therefore it is certain that *neither extensive marshes, nor putrefaction, nor the mixture of salt and fresh waters are conditions indispensable for the local production of malaria.*

The most favourable and most common condition is, we repeat, still or slowly running spring water.

The Roman Campagna teaches us this in an undeniable manner.

If we cast a glance over fig. 27, which represents a section of it, we see on the one part the Latial Mountains, the remains of the ancient volcanoes, now the Lakes of Albano (A) and of Nemi (B); on the other the Lake of Bracciano (C), and between them an undulating plain to the valley of the Tiber (D). (E) represents a diagrammatic section of the Latial volcano.

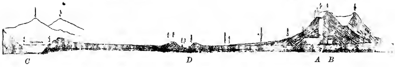
From this to the valley (F) of the Anio or Teverone, one sees the ground broken up by very many low hills. These hills of the Agro Romano (see pages 3 and 4) are chiefly formed of tufa, which, gradually disintegrated by atmospheric agents, has given rise to a stratum of humus which in former times was much thicker, but to-day, especially on the higher parts of these hills, is very thin; it is, however, thick in the valleys, where it has been washed down by the rain-water.

The tufa, being a soil containing very fine pores, is readily impregnated with water, but it permits little of it to pass through. Di Tucci and Tommasi-Crudeli have demonstrated that the rain-water readily stagnates in it, and under the humus forms sheets of water or thin subterraneous marshes; then, descending and collecting in the valleys, it forms true marshes. There is thus a *circulation of the surface water*, especially as wherever the soil is porous large quantities of rain-water are absorbed, afterwards reappearing as small springs or temporary marshes from the autumn to the end of spring, and without being influenced by the deep circulation.

For the local production of malaria, the *circulation of the deep water* is, however, much more important.

It is known that here in the subterraneous zone there is an enormous amount of water. Some authorities maintain that from the Lakes of Albano and of Nemi, as is seen (fig. 27) in the geological section from the Latial hills to the Teverone, a continuous filtration of water takes place towards the valley. It is more certain that the whole of the

GEOLOGICAL SECTION FROM THE LATIAL HILLS TO THE TIBER AND THE LAKE OF BRACCIANO



GEOLOGICAL SECTION FROM THE LATIAL HILLS TO THE TEVERONE

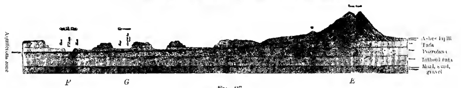
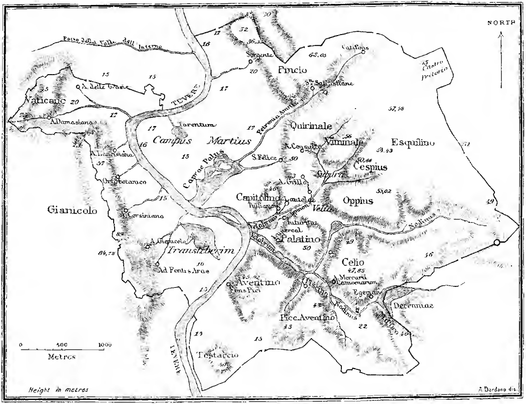


FIG. 27

absorbing basin of the Latial hills, with their large enclosed valleys, the crateriform depressions of the extinct volcanoes, serves as an enormous reservoir, absorbing above and filtering at the bottom, where the waters encounter the stratum of pozzolana which concentrates and leads them to the valley of the Teverone. The sources of the *acqua Vergine*, for instance, are situated in the valley called Salone (fig. 27 *a*), where by means of wells and tunnels an enormous quantity of water is collected which daily comes to Rome. So also the *acqua Felice* is a local manifestation of the water that filters from the Latial volcanic mountains, and is carried in the open along a stream of subterraneous lava.

Similarly the ground-water of the Agro Romano is very abundant, and rather superficial in the low-lying areas. Here, in whatever spot one excavates, a perennial flow of water is found. And thus an enormous subterraneous liquid stratum traverses the subsoil of the city of Rome. Figure 28, taken from Lanciani, shows the numerous springs that existed in the small perimeter of the city, and how they made their appearance in the bottom of the valleys, then running on the surface or collecting in marshes or ponds. This figure may be taken as an exact picture of a great part of the Agro Romano. In a section of the city (fig. 29) we see at A-B the profile of the aquiferous zone, or the level of the ground-water from the Janiculum to Porta San Lorenzo. In some spots this water runs very superficially; for example, at the bottom of the Janiculum


NORTH
Fosso della Valle dell' Inferno
Vaticano
A. delle Grazie
A. Damasiana
A. Lancisiana
Orto botanico
A. Corsiniana
Gianicolo
A. Gianicolo
Transtiberim
Ad Fontis Aras
TEVERE
Tarentum
Campus Martius
Caprae Palus
Sorgente
Pincio
Catifons
Castro Pretorio
Petronia Amnis
Quirinale
Viminale
Esquilino
A. Consulta
S. Felice
Cespius
Subura
A. Grillo
Capitolino
Tullianum
Velia
Oppius
Spinon
Tutumae
Lupercal
Palatino
Velabrum
Nodinus
Celio
Aventino
Fons Pici
A. Mercurii
Camoenarum
Egeriae
Piscina
Picc. Aventino
Decenniae
Testaccio
0
500
1000
Metres
Height in metres
A. Dardano dis.
30
32
56,33
12
16
20
15
15
25
20
12
17
17
16
15
57
89
84,75
10
17
15
65,05
15
57,78
56
53,43
50,66
50
43
46
53,02
49
51
50
49
47,85
45,92
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43
43
46
22
46
15
15
50

Fig. 28.

PROFILE OF THE AQUIFEROUS ZONE OF THE CITY OF ROME

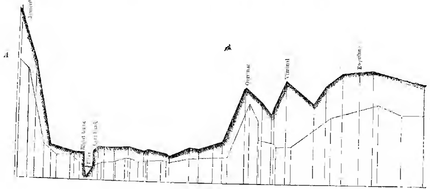

Fig. 29

it appears at the surface, and it is frequently swampy there. On the Quirinal the water follows the ascent of the hill; on the contrary, on the Viminal it descends very low. In this way Tommasi-Crudeli correctly explains, in all the Campagna, the singular perennial flow of our rivers, the abundance of the springs and streams or so-called *marrane*, the extraordinary abundance of the ground-water; and he likewise explains how this soil, when it rains, is full of marshes which during a part of the summer become dry, but when it rains are quickly re-formed.

This author, then, justly maintained in 1879 that Roman malaria was due not so much to the few large marshes as to the thousands of small marshes scattered over all the country round Rome.

To-day we can thoroughly understand the reason, knowing that stagnant or almost stagnant waters are the nest of the larvæ of the malarial mosquitoes.

And one also understands that an hydraulic sanitation, which would radically correct these natural conditions, would be an enormous work, almost beyond the powers of man; and therefore one understands how malaria has reigned in the Roman Campagna for centuries.

But we shall see that there are some other causes for the humidity of the soil.

Even independently of the local rains and of the subterraneous waters, marshes are formed by the rivers that, from their source to their mouth, may be the cause of inundation of the soil, and consequently of malaria. At its sources in the mountains, where there are no woods, during every heavy rainfall the river swells, overflows its banks, and bursts into the plain; therefore, we also accept the idea that woods and forests in the mountains should be considered sacred and inviolable. In the valleys, also, a watercourse may expand, owing to there being a slight fall into the sea. For example, the very large amount of water of the Pontine Marshes (see fig. 25) cannot discharge itself directly into the sea, because along the shore a wide sandbank is interposed; hence the watercourses have to take a very circuitous route to the south; and in this channel the fall is so slight that the water appears almost stagnant. Discharging canals, as we shall see, have been constructed, but they are insufficient, so that in the season of heavy rains the rivers swell, a great part of the region is inundated, and the marsh re-forms there.

Along the Tuscan littoral another phenomenon happens: the waters go directly into the sea, but they are driven back by the sea currents, and thus the marshes are formed.

Morasses or marshes, and true lakes, are also formed by the welling up of the subsoil water to the surface. For instance, if a hollow be surrounded by mountains, and if in that place the subsoil water be abundant, it collects in the hollow, is increased by the rain-water of all the basin, and forms a lake or a marsh according to circumstances. One also has marshes and true lakes of more or less salt water, when the sea water passes through a tongue of land along the coast, or passes over it during high tides.

The fact has been known for a long time that around these marshes and lakes malaria develops most in the period when the waters recede.

Well, how can this fact be explained by the new theory of the genesis of malaria in the environment?

First of all, this period is the fever season everywhere; that is to say, it is the period in which the temperature predisposes notoriously to the development of malaria.

And then, when the water begins to recede, many mosquitoes have already become mature. If the larvæ have already developed into nymphæ, the water can completely disappear, for the nymphæ develop into adult mosquitoes in earth even better than in water. But if, as frequently happens, after the fall of the waters, a small quantity remains permanently, the life of the larvæ continues to be maintained, assuring at the same time the perpetual reproduction of the species.

Consequently, a more minute study of the life and habits of the malarial mosquitoes will give us increased knowledge concerning the epidemiology of the disease.

Air.—This also has very great importance among the local predisposing factors of malaria; therefore soils can be made healthy by withdrawing or limiting the free and direct access of this factor on the surface of the earth, which, as we shall see when speaking of drainage, can be brought about in diverse ways.

That the air has all this importance can be easily demonstrated by repeating an old experiment of Lancisi. He obtained some marshy water containing the larvæ of mosquitoes. And this is what he says: '*Vermiculos qui aperta in phiala mirabili agilitate movebantur; quique si invicem piscium instar movebantur; mox eadem diligentissime per ceram, quam dicunt hispanicam, clausa brevi motum amisisse*' (loc. cit.).

We have repeated this old experiment under rigorous anaërobic conditions, and we have seen that the larvæ and nymphæ really die in ten to twelve hours. And this occurs because the larvæ, and still more the nymphæ, require, as we have said, plenty of air. In fact, to kill them it is sufficient to limit the free afflux of the atmospheric air, for, as we shall see, oily substances spread out in a thin layer on the surface of waters, act mechanically by preventing the free exchange of atmospheric air, and thus asphyxiate the larvæ and nymphæ of mosquitoes.

Therefore the presence of air is indispensable to the life of the malarial germs in the environment, inasmuch as it is indispensable to the life of the larvæ and nymphæ of mosquitoes in water; and any soil is capable of becoming malarious when the water and the air, and certain conditions of vegetation, as we shall presently see, concur in enabling the malarial mosquitoes to live.

In the absence of the above-described local conditions mosquitoes could not develop, and then there would be no malaria.

We shall now briefly describe other local conditions that are associated with the development of malaria; we shall speak, first of all, of the **relations that exist between agriculture and malaria.**

Does the ploughing or digging up of a soil, or other similar agricultural operation, cause the development of malaria? During the time in which it was held that malaria was imprisoned in the ground in the form of a micro-organism, it was believed to be very dangerous to disturb the soil, and cases of malaria were frequently mentioned as being caused by excavating the ground. But to-day we cannot accept this theory purely and simply; for even in soils of malarious localities it is not so much the mere *disturbance of the soil* which influences the production of malaria, as that every such disturbance, which in any way alters the hydraulic state of a given surface leading to the retention of the water, becomes in reality a local predisposing cause to the development of malaria. For example, if a watercourse, even a small one, be interrupted, or if a hole be made in the ground, where the rain water or the subsoil water collects and cannot run away, there the whole aquatic life-cycle of the mosquitoes can very well develop during the appropriate season, and in a short time.

Is the so-called *paludal vegetation* necessary for the life of the larvæ in water, that is to say, that *ensemble* of plants which develop in marshy places, and sometimes cover the surface of the water like a green carpet?

For the common mosquitoes it is known that it is not necessary; they deposit their eggs in all kinds of water; the *Anopheles*, on the contrary, prefer clear waters rich in marsh plants, such as reeds, rushes, cresses, and especially *algæ* such as the *confervæ*, possibly because this kind of vegetation above the surface of the water affords shelter to the larvæ from the wind, heat, and cold.

Among the agricultural operations which favour the development of malaria, irrigation must first be mentioned. For instance, the irrigated meadow lands, the so-called *marcite*, which are very common in Lombardy, are fields carefully levelled, with afferent and efferent channels for the flow of water; forage plants, especially the *leguminosæ*, are grown in them, and they are highly manured. In these fields the vegetation is very rich, so much so that in good climates such as ours they yield eight to ten crops a year. Examples of this kind of cultivation exist also round Rome; some lands reclaimed by the Lombards, as at Cervelletta and Bocca di Leone, for example, are cultivated by this system.

When the water enters the afferent channels it spreads over the field, part of it is absorbed, and the remainder runs away in the efferent channels in a continuous flow; and if the land be permeable so as to absorb the water quickly, this method of irrigation is not liable to produce malaria; the mosquitoes do not deposit their eggs there, and the larvæ cannot live. But in practice it often happens that the water stagnates or becomes sluggish in one or other channel, so that the larvæ can live and eventually develop into malarial mosquitoes.

It is true, however, that this method of cultivation does not require much attention from man. After the irrigation is started, if all goes well, he need only go there from time to time to regulate the flow of water and to reap; if, however, he dwells within a certain radius, he is affected by it.

In former times (see p. 10), here in the Campagna, irrigation was regularly established in the valleys of the Arrone, Aniene, and Galera, by means of expensive masonry work and suitable levelling of the soil.

Any one who visits many of our valleys, in which water is always present, frequently finds there such works, together with extensive stalls for milch cows and large buildings for cheese-making, that he must come to the conclusion that, at a time not very remote, the agricultural activity was very different in these valleys from what it is to-day.

Why this industry was abandoned it is not easy to answer. But it is certain one cannot consider it likely that it was unprofitable. Therefore I am strongly of the opinion that malaria of milch-cows and of man was the cause of its destruction.

The irriguous cultivation of some other crops is much more dangerous, as that *of rice*, for instance. The map of the rice fields in Italy demonstrates that it is chiefly carried on in Northern Italy, and in the valley of the Po; it is also common in Sicily, in the province of Campobasso and of Naples. From the statistics compiled in 1881 we take the following figures:—

	Hectares
Land irrigated in Italy	1,500,000
" cultivated with rice	200,005

But, what is worse, there is a tendency to extend this industry, which is very remunerative; there are already some instances of it in the Pontine Marshes. Now it is certain that, in some places where malaria had disappeared for a long time, it has made its reappearance with the cultivation of rice. Thus the valley of Potenza, near Macerata, previously healthy, became malarious after the cultivation of rice there; indeed, so bad was the disease that this culture was suspended by governmental decree. One of the proprietors insisted on continuing it, but the people rose up in arms, and the last remaining rice-field was destroyed.

Also from the investigations already mentioned, made in the province of Parma, the injurious influence of rice-fields on the production of malaria, even when these are in sites of mild or latent malaria, is undeniable. Imagine what must happen in sites of intense and severe malaria!

After what we have said of the life of the *Anopheles* larvæ in the environment, it is evident that rice-fields with their clear and slowly running waters and their typical paludal vegetation are the best habitat of these larvæ, that is, the best they could wish to live in.

There are, it is true, different kinds of rice-fields.

A primordial type, which is adopted in all low-lying places, where the water stagnates, and where, after the smallest rainfall, marshes form, is that of the *risaie di ventura* (rice-fields of chance), called thus because they are made by the goodness, the chance, or the *mercè* of the water that falls and stagnates there.

A second type is that in which, in low-lying land, the water collects in basins, where it is retained by means of dykes, into which the water enters on one side and runs out at the other. The rice is continually submerged, and the water is always clear and running. This is the type of *rice-field with continuous submersion*, with running water.

A third type, in which the submersion is made for two to three days in the week (on the other days the rice-field is kept dry), is called *risaia a vicenda*.

The first type need not be discussed, inasmuch as it undoubtedly constitutes a local condition favourable to the development of malaria.

The other two have been studied accurately to see how and to what extent they are propitious to the life of mosquitoes. And now we can say that the rice-field of the second type is an excellent nursery for larvæ, including those of the *Anopheles claviger*; these made their appearance in the second half of May, increased in number by successive generations, and continued to be abundant till the water was let off for the reaping. The larvæ of the *Culex penicillaris* and *annulatus* made their appearance after those of the *Anopheles*.

From what we saw in Table III., we were able *a priori* to maintain that the larvæ would survive the brief dryings of the rice-fields of the third type. And, in fact, this has been found to occur.

The movement of the water, even when the supply is abundant, does not free a rice-field from the larvæ. These escape from the parts where the current is strongest and take refuge in those where it is weakest or where the plants are thickest. It is not possible, therefore, to render a rice-field healthy by the movement of the water.

But to better understand the relations between rice-fields and malaria, it is necessary to describe the different agricultural operations, which in the various seasons require the presence of man, according to the ordinary and more rational method of culture.

In the early spring they begin to divide the land into squares. The water finds its own level, and according to this level a number of squares are made which are surrounded with banks of earth of sufficient height. The afferent and efferent channels for the water are also systematically arranged in such a way that in every square the water enters through an opening in one of the banks and runs out through another opening in the opposite bank. This afflux and efflux is easily regulated by slight movements of the earth. Inasmuch as the water when it enters is cold or fresh, and the low temperature injures the plants, it is advisable to alternate the entrance and the exit of the water.

The rice is sown under water at the end of March and in April. The water is then cut off for a short time in order to permit the young and small plants to take root.

The weeding is also done under water in May and June.

During the growth of the plants the continuous or intermittent submersion is, as we have said, maintained. This in very rich ground is injurious, because it makes the stalks grow too tall, to the detriment of the crop; it is beneficial, however, in poorer soils for strengthening the plants; so that even if it be hygienically advantageous, it is not always so from the agricultural point of view. And therefore it is not always possible to obtain a complete drying of the land.

In fact, it may easily happen that the field remains either wholly or partly saturated, or that small collections of water remain in the tracks made by man or animals during the agricultural operations, or where the soil is not properly levelled. In these spots the larvæ develop undisturbed.

For several months the presence of man is required only to look after the water-channels and to repair the banks often perforated by rats. But many men are required for the reaping, which takes place, according to the quality of the seed, in August, September, or October, in dry or saturated ground, but no longer under water. Then the mosquitoes rise in swarms, especially in the evening hours.

After the reaping the water is either entirely cut off, and the ground becomes completely dry, or it is retained for macerating the stubble and thus obtaining a kind of manure; in this latter case, and sometimes also in the former, the water remains in the hollow parts and continues to be the habitat of the larvæ of the *Anopheles* mosquitoes—in our climate during the whole winter.

Some authorities hold that rice-fields of every description are permissible in all places more or less submerged, because the soil is already marshy, and if malaria appear there after the making of the rice-field, it was there before. Furthermore, they have proposed to convert marshy places, including many parts of the Pontine Marshes, into rice-fields.

But it must not be forgotten that the cultivation of rice, besides requiring more or less the presence of man, especially during the weeding and gathering of the rice, makes its injurious effects felt at a distance. Moreover, if rice-fields be instituted on a large scale, hydraulic sanitation will never be carried out. And then malaria undergoes annual variations through various causes; for example, in very dry years, in consequence of many collections of water being dried up, it becomes attenuated, while with the rice culture system the infection would be every year more regular, and therefore more severe.

So that extending this culture of rice in malarious regions, and, worse still, in those of severe malaria. is an absolutely reprehensible proposal; and it is to be hoped that private interests will not outweigh those of public health.

It is believed by some that the *culture of textile plants* also has direct correlation with malaria. Some of these plants grow in dry soils, but then they require to be submerged and macerated in water when they have been gathered, as, for instance, hemp and flax.

The culture of hemp and flax is sufficiently widespread in Italy, as is revealed by the following statistics for 1881, collected from the principal regions where these textile plants are grown :—

TABLE VII

	Hemp. Hectares.	Flax. Hectares.
Emilia	72,182	1,584
Venice	11,131	1,589
Lombardy	3,432	36,268
Piedmont	4,671	145

From the above it is seen that hemp is much cultivated, especially in Emilia, while flax, like rice, is especially so in Lombardy.

The maceration of these plants is carried out in various ways, but generally as follows : If the subsoil water be very superficial, a trench is dug to collect it, and the plants to be macerated are placed in it. If there be a stream or streams in the land, the water is diverted from its bed and collected in basins, where the plants are placed to macerate. The vegetable putrefaction which develops separates the textile fibres.

In both cases, however, it is doubtful whether this maceration constitutes an environment *per se*, favourable to the development of the malarial mosquitoes, and, consequently, of malaria. We have said already that these mosquitoes, unlike the Culices, do not by choice deposit their eggs in putrid waters, and we may now add that their larvæ soon die in the waters in which these plants are macerated.

Nevertheless this agricultural operation, when watercourses are employed, may produce stagnant pools favourable to the life of the specific mosquitoes, even beyond the site where the maceration is carried on; and, *vice versa*, when it is performed in large tanks of masonry, and especially if these tanks be constructed in such a manner that the water is constantly running, very probably the specific mosquitoes will not develop in them. This question, however, requires further study. It is certain that in some regions they practise this maceration without the development of malaria, as it is also certain that while the macerating waters are favourable to the development of the *Culex* larvæ, they are, on the contrary, as we have said, the grave of the *Anopheles*. Therefore the dread which they inspire as foci of this disease is also the result of the prejudice that has so long prevailed in the medical schools, regarding the decomposing swamps as being the cause of disease, and especially of malaria.

Among the various plants which grow in humid soil, *canes* merit special mention. These, in the Roman Campagna, in the valleys where they are planted along the watercourses, form most suitable breeding-places for mosquitoes, including the *Anopheles*.

On the other hand, the irriguous culture of *agrumi* (oranges, lemons, citrons, and limes), so extensive in Calabria and Sicily, appears (as it is usually carried on) to have no injurious influence as a source of malaria. It nevertheless requires to be better controlled.

In general, is the *temporary irrigation of the* *soil* in unhealthy localities injurious or not? It probably is not if the water flows freely and is never obstructed in the irrigation channels, and if it be quickly absorbed by the soil, like a slight fall of rain. This subject is so interesting that it also merits special study on the lines of the new etiology.

Is the *arboriculture* of a malarious territory favourable or not to malaria?

What we have already said of Lancisi, *à propos* of the Cisterna woods, will be remembered.

As long as Lancisi lived, he, owing to his great authority, prevented these woods being cut down; but after his death the disforesting began, and was continued almost to our time. And to-day, instead of woods, vineyards flourish round Cisterna. Well, not only has that prevalence of the malarial epidemy predicted by Lancisi not occurred, but, on the contrary, there has been such an improvement there that in the middle of the square a monument has been erected to the defeated goddess Fever.

In 1808, Santarelli, also a Marchigian physician, wrote: 'The history of many regions collected in the whole world combats such an opinion' (Lancisi's), 'and shows that those lands, now healthy, before the woods were cut down were unhealthy.'

The new etiology fully confirms these theories. In fact, we have said that mosquitoes thrive extremely well in woods, where they take shelter from the heat of the sun or from strong winds. Still more, there are some which are really wood-lovers, such as the *Culex nemorosus*, and, of more interest to us, the

Anopheles bifurcatus, which live preferably in thickets; so that any one who sleeps in them, even during the day, generally in a malarious spot, very easily catches the fevers during those periods of the year when they prevalent. In certain woods, in the summer, it is impossible to pass through them during the day, owing to the enormous numbers of insects, and among them mosquitoes, which attack men and animals.

Our woods along the coast rarely consist of true trees with high trunks, so that the evaporation of the subsoil water can take place rapidly, but of thickets in saturated soils that remain humid and even marshy in the hottest and driest summers. These woods surely are not to be considered sacred!

In 1884 a Commission was nominated which studied in our coast-line regions the influence that disforesting had on public health. They state that 'in all the visits made and inquiries undertaken at all these places in the Roman province, where sanitary reports, complaints of communes, and publications issued during these last eighty years, assert that the total or partial destruction of woods, thickets, and hedges had occasioned an increase of malaria, after careful investigation, not only were they unable to find any proof that disforesting was injurious to health, but they found that some facts indicated an opposite effect.'

'In fact, in the places where the woods have been destroyed or diminished malaria has not increased; and, furthermore, in some places it has become mitigated as the result of improved agriculture in the Campagna, and, above all, by the better system of drainage.'

'On the other hand, no example has been found of a new plantation of trees of any extent which has produced a diminution of malaria in the neighbouring habitations.'

The woods should therefore be respected on mountains and hills, because it is certain that if the mountainous regions from which the watercourses originate be disforested, at every heavy rainfall there will be flooding in the plains. In the low and marshy regions, on the contrary, where malaria exists, they certainly favour the development of this epidemy.

Even popular experience in some malarious places is decidedly inimical to trees. It is not rarely that one hears it remarked that they harbour malaria—this can be explained now by the fact that they are the favourite resort of mosquitoes.

But is there any plant hostile to malaria or to the mosquitoes, so that its cultivation in a territory will protect it from them?

The *eucalyptus* planted round our railway stations are now proved to be useless against malaria, if even they do not do more harm than good by harbouring the mosquitoes near the houses. Here outside the gates of the city, at Tre Fontane, an intensely malarious spot, there is a fine wood of them; and in Australia there are immense forests of these trees, and all are malarious.

Professor Cantani, in his splendid book 'Pro Silvis,' maintains that plantations of pines, firs, are antimalarial, because, as he has written, by these trees giving off ozone the malarial germ would be destroyed. This explanation to-day no longer holds; and besides, in the neighbourhood of Rome, there are magnificent pine woods in intensely malarious sites, as, for instance, at Castel Fusano near Ostia.

Up to the present we know no plant inimical to mosquitoes. The *Ricinus communis*, which has been extolled as a culicifuge, and other plants such as *Iris fœtidissima*, *Delphinium Staphisagria*, *Sambucus ebulus*, *Chenopodium Vulvaria*, *Solanumnigrum*, *Pistacia Lentiscus*, *Daphne Gnidium* afford, on the contrary, as we ourselves have seen, an excellent refuge for mosquitoes. Nevertheless, it is not impossible that plants may be found that give off an odour noxious to these insects, which, as is known, have a very keen sense of smell. For example, the Roman wormwood in flower is capable of causing, in a closed chamber, their apparent death in six hours, and actual death in twenty-four hours. The other wormwoods or *Artemisiæ* exercise a similar, but not such an energetic, action.

Finally, we shall say a few words of the relations between malaria and *intensive culture*. *Market gardens* are a type of this culture. Around Rome we have a number of splendid examples of these market gardens, situated in valleys which formerly were malarious, but now seem to be healthy. This also is a subject for study. For the present it may be said that we have found the so-called garden mosquitoes, that is, those which prefer market gardens, such as the *Culex hortensis*, *C. annulatus*, and the very common *C. pipiens*, always in abundance in these places; but in the middle of summer the *Anopheles* have also been found developing among the other larvæ in somewhat turbid water. Generally, in highly cultivated soils it is necessary to regulate the surface and ground waters respectively. The soil must be rendered very permeable. This system of culture may be useful also from the hygienic point of view, correcting the hydraulic regime, which is a potent local predisposing cause of malaria, without, however, altogether suppressing it. Unfortunately, this system is difficult to carry out in unhealthy places. Large estates and malaria usually go together, because man, in certain months of the year, cannot live in intensely malarious regions, where, therefore, only cultivation on an extensive scale is possible, and hence the large estates.

With regard to the association of malaria with special industries, we have principally to consider the *fish-ponds*, the *saline marshes*, the *peat bogs*, and the *railways*.

In speaking of *fish-ponds* in malarious localities, we shall mention those of fresh water, such as the canals which discharge into the valleys of Comacchio along the Adriatic coast, and those of salt water along the Tyrrhenian littoral, as the Lake of Fogliano in the Pontine region, for instance.

That fresh-water fish-ponds in a malarious locality favour the development of malaria can be very well explained by the new theories. We know, on the other hand, that fairly strong salt waters are not favourable either to the malarial or the non-malarial mosquitoes. The waters of the Lake of Fogliano, for example, have scarcely 1·33 to 0·15 % of salt—that is, much less than sea water—and consequently the larvæ of mosquitoes live and develop there. Again Lake Trajano, near the delta of the Tiber, in the Isola Sacra, contains only 0·427 gr. % of sodium chloride.

But in Italy we have also *salines* much infested with fevers, that of Cervia near Ravenna, and that of Corneto, on the Tyrrhenian littoral, for instance.

Now it is necessary at once to note that these two salines are situated in a littoral territory surrounded by malaria.

We have already seen how the larvæ act in sea water, and we shall see now how they act in salt solutions of various strengths.

We may state briefly that the larvæ, both of common mosquitoes and of *Anopheles*, in a 5 % solution of salt—which is about double the quantity found in the Mediterranean water (the mean is gr. 2·722 %) —die in about two hours if they be very young, after fifteen hours if full grown; the larvæ of *Anopheles* dying sooner than those of the common mosquitoes. In saturated solutions of salt the larvæ die in half an hour, and the nymphæ in the short space of an hour.

In the salines the water, by evaporation, constantly becomes more concentrated and certainly injurious to mosquitoes, and it will be necessary to see whether they get habituated to such conditions of life, originally so unfavourable.

And then around the salines, as at Corneto for example, there are many stagnant, or almost stagnant, fresh collections of water, in which all the mosquitoes that infest that malarious place can develop. And, in fact, the larvæ were found in a wide trench which surrounded the salines and intercepted the fresh water and conveyed it to the sea. In this canal the larvæ were found in the parts opening into the sea where the salt was 1·39 %; however, they were not found nearer the sea, where the salt was 2·09 %, as *a fortiori* no larvæ of any species were found in the basins of sea or concentrated water. So that up to now we can say that the salines *per se* do not constitute a local condition favourable to the development of malaria.

I remember, on the contrary, that the sea water alone penetrating into that malarigenous canal near Sinigaglia (see p. 82) was sufficient to render healthy that small circumscribed focus of malaria.

But as early as 1803 Morichini had arrived at the same conclusion as regards the saline of Corneto, Ramezzini and Cervia, and Lancisi held the same opinion about salines in general.

As to the *peat bogs*, it is known that they are old marshes which, in the course of time, became filled with decayed marsh plants which were undergoing fossilisation. On removing the peat the pools of stagnant water, in which the rank vegetation quickly forms, are the most favourable local conditions for the production of mosquitoes, and consequently of malaria, where this disease prevails.

Frequently also the *railways* are *fomites* of malaria amongst us. They for the most part run on low lands, and are, therefore, frequently malarious. In the construction of the lines, cuttings and embankments are made, and consequently the level of the subsoil water of a district is altered, the water-courses are intercepted, and marshes and morasses are produced.

Very pernicious also are those so-called *cave di prestito* (pits from which soil is obtained for making embankments), which are deep, and have no outlet for water, and are so much used and abused by our railway contractors. Thus many sites are created suitable for the development of mosquitoes, and therefore of malaria. Indeed, after the construction of the railways, malaria became widespread among us even in some territories which before were little or not at all infested; and in those that were malarious, it was frequently aggravated, especially during the first years of construction.

We shall now see what are the other local causes which regulate the epidemic course of malaria, namely, the

INFLUENCE OF SEASON

There is no doubt that the seasons have an influence on the production of malaria; so true is it, that malarial fevers are commonly called after the particular seasons during which they prevail.

Lancisi has also indicated this correlation, observing that '*Itaque principio æstatis febres ut* *plurimum non malignæ corripiunt: adaucto vero æstu, febres continuæ, atque etiam exitiales urgent; longe tamen deteriores evasuræ, et plane pestilentes circa æquinoctium autumnale, præcipue si pluviæ, nebulæ, rubigines, ventique australes accesserint. Tandem circa hyemale solstitium de pernicie ubique remittunt; sed in chronicas affectiones abeunt: qui enim ab ejusmodi febribus liberantur, fere semper contumacibus viscerum obstructionibus et quartanis longo dein tempore duraturis divexari solent.*' (Chap. XI.)

At the time of the French occupation of Rome, Colin, one of the most distinguished army surgeons, made a study of the health of the troops in respect to this epidemy; and, collecting many data from 1845 to 1865, he came to the conclusion that in the first six months of the year there are relatively few cases of malaria; afterwards, in July, a true epidemic breaks out, which reaches its maximum in August, and then declines during the succeeding months to the end of the year.

In its broad lines the phenomenon proceeds in this way, but in the details there is much to add.

To give an exact idea of the course of the fevers in the various months of the year, in Table VIII. is collected, month by month, the total number of cases observed in the hospitals of Rome in the years 1864 and 1865, 1873 and 1874, 1877 and 1878, and then from 1892 to the end of 1898.

This table includes an enormous number of cases of fever, namely, no less than 93,000.

On account of the oscillations that the labouring

TABLE VIII

Months	Years													Total
	1864	1866	1873	1874	1877	1878	1892	1893	1894	1895	1896	1897	1898	
January	284	195	853	595	638	661	240	189	249	236	314	129	90	4673
February . . .	228	198	681	528	519	543	177	125	168	175	243	94	58	3782
March	189	170	711	747	544	502	231	119	125	165	244	98	61	3906
April	168	151	653	675	564	576	223	148	157	180	235	115	76	3921
May	112	114	669	584	480	504	244	119	159	165	229	120	76	3575
June	83	88	409	331	339	375	205	119	138	150	155	88	73	2553
July	439	340	1135	865	1858	398	608	553	813	582	502	320	431	8844
August	1492	570	2824	2647	2373	1604	694	741	1298	1181	939	410	905	17678
September . . .	1056	476	2185	2019	1995	1896	586	761	984	1357	684	505	799	15203
October	775	437	1761	1732	1460	1495	500	911	855	1191	532	403	703	12755
November . . .	431	475	1280	1186	795	1245	404	831	678	898	361	215	732	9531
December . . .	271	205	777	773	695	1193	311	427	427	767	252	137	386	6621
Total . . .	5528	3419	13938	12682	12260	10992	4423	5043	6046	6947	4690	2634	4390	92992

population, which is most subject to malaria, underwent during the time of the building fever (1873–78), and during the crisis from 1892 onwards, this table gives us no information concerning the annual periodical course of this epidemy; it, however, furnishes us with a very exact idea of the monthly course.

We see at once that malarial fevers are present in the hospitals during the whole year.

In the first six months of the year, with some slight variations in March and April, the cases are relatively few, with the maximum in January, the minimum in June. In July, towards the first or second decade, there is a sudden change; the true epidemy of malaria breaks out, reaching its maximum generally in August, but some years in September, and even occasionally in October. In thirteen years the maximum occurred nine times in August, three times in September, and once in October.

Generally, the epidemy declines in October, and is much reduced in November and December; but in some years—in 1878, 1893–94, and 1898—it has been prolonged and maintained high even in the last three months of the year. So that the true epidemy of malaria occurs in the second half of the year.

In these latter years the clinical observations have been made with greater accuracy, the examination of the blood has been taken into consideration; and, with the statistical investigations introduced by Ballori, distinction has been made between primary and

TABLE IX.—CASES OF PRIMARY, RECURRENT, AND PERNICIOUS MALARIAL FEVERS IN THE ROME HOSPITALS

Months	Years																					Total		
	1892			1893			1894			1895			1896			1897			1898					
January .	57	*183*		83	*105*	1	174	*75*		179	*57*		208	*105*	1	84	*45*		79	*11*		864	*581*	2
February .	62	*115*		68	*57*		98	*65*		136	*39*		193	*49*	1	67	*27*		52	*6*		676	*358*	1
March .	107	*124*		86	*33*		90	*35*		127	*38*		176	*68*		82	*16*		56	*5*		724	*319*	
April . .	115	*108*		98	*50*		118	*39*		151	*29*		135	*100*		103	*12*		73	*3*		793	*341*	
May . .	150	*94*		83	*86*		122	*37*		116	*49*		163	*66*		105	*15*		70	*6*		809	*353*	
June . .	128	*77*		78	*41*		113	*25*		101	*49*		127	*3*		80	*7*	1	69	*3*		696	*205*	1
July . .	445	*160*	3	456	*84*	13	688	*114*	11	520	*58*	4	421	*77*	4	301	*15*	4	81	*14*	6	2912	*522*	45
August .	510	*173*	11	590	*144*	7	1024	*261*	13	1005	*170*	6	798	*128*	13	375	*31*	4	855	*42*	8	5157	*949*	62
September .	349	*226*	11	557	*178*	6	751	*223*	10	1013	*225*	19	566	*110*	8	460	*43*	2	744	*26*	11	4440	*1031*	67
October .	304	*187*	9	699	*201*	11	612	*239*	4	827	*352*	12	445	*80*	7	357	*37*	9	631	*60*	12	3875	*1156*	64
November .	248	*152*	4	617	*209*	5	510	*163*	5	637	*245*	16	226	*133*	2	172	*39*	4	664	*48*	20	3074	*989*	56
December .	151	*158*	2	294	*133*		308	*115*	4	559	*199*	15	170	*80*	2	119	*19*	1	366	*12*	8	1967	*716*	32

recurrent fevers, and between ordinary and pernicious fevers. In Table IX. the numbers printed in ordinary type represent cases of primary fever; those in italics. cases of recurrent fever; and those in heavier type, cases of pernicious fever.

If we take the total of the monthly observations of these years 1892–98, we find that in January an occasional case of pernicious fever is still observed, and also in February.

But in March, April, and May pernicious fevers never occur; and it is also doubtful if they occur in June, inasmuch as the case which figures in 1897 was not confirmed by finding the parasite in the blood, nor by the autopsy; and consequently we are not at all certain about the diagnosis.

The primary infection of severe or æstivo-autumnal malaria begins regularly in July—in which we have in various years 45 cases of pernicious fever—increased in August to 62 cases, and in September to 67 cases; it commences to decline in October to 64 cases, in November to 56 cases, in December to 32 cases, and ends in January and February with 2 and 1 cases respectively.

There is therefore a very distinct interruption that generally extends from March to July.

On observing more closely this course of the primary infections, we find, from the above statistics, that in January we have still a notable number of primary fevers, but also a very notable number of recurrent fevers. And while in February, March, April, and May the number of relapses remained more or less constant, in February and March the primary fevers become somewhat diminished, increasing again in April and May, to diminish in June. But in reality I am not by any means certain that all these fevers indicated as such are primary; on the contrary, I believe that the majority of them are long-interval recurrent fevers.

In July, towards the middle, as a rule, or a little after, there is suddenly a great predominance of the primary fevers, generally of the severe æstivo-autumnal form, and to a less extent of the spring form. This is the beginning of the true epidemic period.

So that with regard to the primary infections, the mild or spring form undergoes a first or slight increase in the spring, a second and greater increase in the summer and autumn. The severe form, on the contrary, has a distinct interruption of four or five months, and reappears in July, continuing more or less till towards the end of the year.

These are the only results to be obtained from the statistics of our large hospitals, but if, as I have done this year with Dr. Del Pino, the individual cases of fever in the same locality are studied daily during the first six months, including an examination of the blood, one finds that almost all the cases of malaria which are met with from March onwards are recurrences with more or less long intervals, sometimes of several months. For example, up to the end of June, in 21 recurrences (12 of quartan, 6 of tertian, 3 of æstivo-autumnal fevers), we have had but one solitary case, which was possibly primary, of mild tertian in April. And at Santo Spirito Hospital Dr. Panichi, studying accurately the individual cases of fever in May and June, has found only cases of recurrences. This agrees exactly with my observations that the labourers who come to mow the hay here in the Campagna in May and in the first half of June do not contract malaria, notwithstanding the life of toil they lead.

In conclusion, *the true malarial season is in the second half of the year; its duration varies in different years; relapses occur during the whole of the first six months of the following year, gradually declining from January to June.*

This holds good for the city of Rome, where, certainly better than in any other city, exact statistical reports are made, and these are controlled by the microscopical examination of the blood.

However, the course of the fevers in northern and in warm climates is not identical; malaria is a distinctly local phenomenon, which develops differently in various localities even when they are not very distant from one another.

Table X. summarises the observations made by Minzi at Terracina. Table XI. summarises the cases of malarial fevers at Corneto Tarquinia.

TABLE X.—CASES OF MALARIA IN THE HOSPITAL OF TERRACINA. MINZI'S OBSERVATIONS FOR ELEVEN YEARS.

January	503	July	829
February	408	August	918
March	407	September	747
April	503	October	627
May	376	November	611
June	377	December	639

Minzi's figures refer to eleven years, those of Corneto embrace twenty years; both give us the number of cases of malaria month by month which have occurred during these two periods.

TABLE XI.—CASES OF MALARIA IN THE HOSPITAL OF CORNETO TARQUINIA, FROM 1878 TO 1899.[1]

January	288	July	299
February	226	August	448
March	198	September	584
April	214	October	639
May	187	November	871
June	185	December	535

At Corneto it is characteristic that the maximum number of cases of fever occurs in November, perhaps because it is in this month that there are a greater number of people in the Campagna.

At Terracina there is a malarial epidemic corresponding to that at Rome, but with a difference; for it would appear that what we may call the spring recrudescence is more marked here. It begins with 503 cases in January, falls somewhat in February and March, then rises again in April, and reaches the minimum of the six months in May and June.

At Cagliari the course of the malarial epidemy, month by month, from 1890 to 1899, was similar to that of Latium, with the maximum, however, in October. Consequently we can speak generally of *a special epidemic type peculiar to warm climates.*

As an example of the annual course of mild malaria in a northern climate, I give the following data, for which I am indebted to Dr. Grandi:

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[1] The data of the first seven months of 1880, the last five months of 1879, and the first nine months of 1887 are wanting.

TABLE XII.—CASES OF MALARIA IN THE MAJOR HOSPITAL OF MILAN, FROM 1894 TO 1898.

Months	Years					
	1894	1895	1896	1897	1898	Total
January . . .	28	26	54	32	91	231
February . . .	30	18	43	27	39	157
March . . .	26	29	59	38	44	196
April	29	38	59	38	67	231
May	41	57	60	40	66	264
June	51	61	91	45	69	317
July	105	75	83	118	93	474
August . . .	122	108	108	181	151	670
September . . .	132	109	96	154	142	633
October . . .	84	145	72	180	171	652
November . . .	108	119	81	106	110	524
December . . .	51	64	62	67	84	328
	Total 4677					

Here also, as in Rome, the maximum number of cases of the fevers occur in August and September. But the minimum of the cases in February and March, and the early recrudescence in April, May, and June, are characteristic, while with us in this last month the disease falls to its minimum. Possibly this slight spring recrudescence occurs also in other places. Thus it appears that in all malarious places there is not that interval of several months in the primary æstivo-autumnal fevers as in Rome. It will, therefore, be very interesting to see how long these fevers are prolonged in the tropics.

And inasmuch as the fevers of Milan have the same course as at Crema, Pavia, and Udini, we can speak of another *special epidemic type of the disease, namely, that of temperate climates.*

Malaria is therefore a local phenomenon which must be studied on the spot; and the data gathered in any particular territory cannot be generalised, or applied to all countries.

Having examined the course of the various malarial fevers during the different months of the year, pursuing our study of the various seasonable conditions predisposing or not to the epidemy, we now come to the **relations between the weather and malaria.**

The first who has made a sufficiently accurate research into this correlation between the individual meteorological factors and malaria is Scalzi, who was for many years Director of the Hospital of Santo Spirito.

His observations refer to the years 1877 and 1878, and take into consideration, besides the temperature, the humidity, barometric pressure, &c. We shall fix our attention on the most important meteorological phenomenon, the *temperature.* One sees at once from the table annexed to Scalzi's work, that the malarial phenomenon in the various months of the year runs almost uniformly during the first six months, and then makes a rapid rise in July and August, to fall again more slowly towards the end of the year. The same table also demonstrates that a real spring malarial epidemy is wanting in Rome.

The course of the mean temperature, during the various months of the year, on the contrary, rises gradually from January to July and August. Consequently the two phenomena of malaria and temperature do not run perfectly parallel; there is certainly a correlation between them, but it is not so simple and direct as some authorities believe.

Hirsch has observed that the zone of distribution of malaria corresponds to a mean summer temperature of 15° to 16° C. (59° to 60·8° F.).

Tommasi-Crudeli has stated that a temperature of at least 20° C. (68° F.) is necessary for the development of malaria. And the recent researches which have been already described have demonstrated that the development of the hæmosporidia in the mosquito's body begins to become possible about this temperature. Nevertheless a rare case of primary fever occurs even in months with a maximum external temperature less than 20° C.; and in May and June, during which the temperature is much higher than 20° C., no malarial epidemy arises. On the contrary, in June it falls to the minimum of the whole year. These apparent contradictions are explained by the habits of the mosquitoes, which have been already described; directly the weather becomes cold, they shelter in the houses, where the temperature is higher, and in May and the first half of June, when even it begins to become warm, they do not commence to bite.

Professor Tacchini, the Director of the Central Meteorological Office of Rome, when he formed part of that Commission which had to study the influence that the littoral woods of the Agro Romano had on malaria (see page 141), compiled the data which are summarised in Table XIII.

TABLE XIII.

Years	Rainfall in the months of March, April, and May	Percentage of fevers in the province of Rome	Mean of the maximum temperature in the months of July and August	Nebulosity of the third quarter. Tenths of sky covered	Number of sirocco days in the third quarter	Frequency of north winds in July, August and September
			Centigrade			
1871	185·8 mm.	6·4	30·3°	2·3	4	0·370
1872	251·3 „	7·1	30·0°	2·5	5	0·328
1873	187·7 „	7·3	32·1°	2·0	5	0·372
1874	225·8 „	5·5	30·0°	2·7	3	0·415
1875	258·7 „	6·2	30·0°	2·9	8	0·341
1876	205·0 „	4·6	29·9°	2·8	2	0·370
1877	191·9 „	4·2	31·0°	2·7	8	0·311
1878	101·8 „	2·9	30·0°	3·5	10	0·337
1879	369·9 „	11·4	29·8°	1·8	1	0·336
1880	209·8 „	8·2	30·6	3·2	5	0·385
1881	227·3 „	6·6	31·7°	2·7	4	0·196
1882	115·7 „	2·5	29·4°	3·0	11	0·200

where in the fourth column are seen the means of the maximum temperature observed from 1871 to 1882 in the months of July and August, and in the third column the percentage of fevers observed in these various years in the province of Rome. We see at once that in the year 1879, when a true malarial pandemic raged, the mean temperature for the months of July and August was the lowest of these years.

We have already mentioned what part some authorities attribute, in the genesis of the fevers, to the variations of the temperature in general, and especially between the day and the night, that is to say, to the daily rise and fall of the thermometer. We have classified the influence of this phenomenon among the predisposing causes which act on the human organism; whether it also affects the life of the malarial germs in the mosquitoes we do not know.

In my case, this meteorological phenomenon requires further study in its relation to malaria. Santarelli, for example, from his personal thermometric observations, has found a diurnal variation of 17° C. Secchi, in his 'Clima di Roma,' gives 17·82°–17·97° C. as the mean variations of summer and autumn, and 33·80°–37·75° C. as the absolute maxima of these seasons. We give for the three hottest days of last summer (August 14–17) a tracing of Richard's registering thermograph (fig. 30), which is regularly at work at Cervelletta. We see that the minimum temperature occurs there after 6 A.M., and the maximum always before noon. The evening, night, and the early morning hours are always cool, even in the hottest days, and the rise of the thermometer from minimum to maximum takes place rapidly from one hour of the forenoon to another.

We have already spoken of the influence of the temperature on the development of the hæmosporidia in the body of the mosquitoes (see pages 61 and 158).

Nevertheless, while in general this correlation between heat and malaria may be admitted, what exactly the correlation is we are at present unable to explain. We can assert in a general way that the course of the temperature must undoubtedly have a very notable influence on the course of the fevers, that is, on their appearance, and on their being more or less prolonged in the autumn and into the beginning of winter.

Whether the temperature has an influence on the sudden appearance of the epidemy in July we do not exactly know; on the other hand, it has certainly been observed that if in the late autumn the temperature falls suddenly—if the cold season sets in early—the primary cases of æstivo-autumnal fevers cease more quickly, and *vice versa*.

Have cold winters and frosts especially any influence on the annual periodic course of malaria, in the sense of regulating the number of insects, and, therefore, also of mosquitoes?

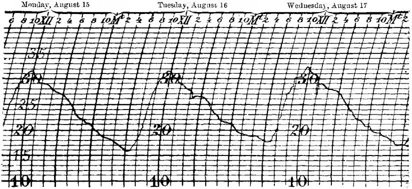

FIG. 30

One sees in Table XIII. that the *rainfall*, with the other meteorological data in relation to malaria, also deserves study.

Professor Tacchini has likewise collected the data of the rainfall for the months of March, April, and May, to see whether there is any relation between the *spring rains* and the malaria in summer.

Well, in the year 1879 there was the greatest amount of rain in the spring and of fevers in the summer. In 1878 there was a minimum of rain and a minimum of fevers.

By the recent researches such a correlation can, to a certain extent, be explained thus: if it rain much in the spring the soil becomes very marshy, and the longer the water remains abundant in the discharging canals and hollows the better the mosquitoes develop, and consequently there will be a greater number of them in the ensuing summer.

The following researches were made by Boldi, the engineer—not for all the province of Rome, but for the zone of 10 kilometres surrounding the city—from 1887 to 1894.

TABLE XIV.

Years	Rain in March, April, and May	Percentage of fevers			Maximum mean temperature in July and August	Nebulosity, third quarter. Tenths of sky covered	In the third quarter	
		Agro	Suburbs	Total			Number of *scirocco* days	Frequency of north winds in a thousand observations
					Centigrade			
1888	216	27	15	17	29°	3·42	5	261
1889	287	23	23	23	30°	2·93	2	278
1890	320	44	22	24	30°	3·00	4	329
1891	157	32	15	17	30°	2·76	4	306
1892	241	14	10	11	31°	2·58	2	327
1893	44	18	8	9	31°	3·76	3	293
1894	218	35	18	20	31°	2·90	3	284

The year 1890 was the wettest in spring and richest in fevers in the summer. But for the other years this correlation between the spring rainfall and the malaria in summer has not always been altogether verified, just as it was not verified by Santori in his study of malaria, in the last decennium, in the province of Rome. Thus the year 1893, with a very dry spring, was more malarious than 1892 with a wet one.

It may very well happen that a considerable amount of rain falls, which, however, for many reasons does not remain on the surface. In 1898, for example, it rained a good deal in the spring; but between one rain and another the ground was always dried rapidly, either by the *tramontana* or by some hot sunny days, so that the ground was as dry as if it had never rained. If, however, in addition to the rain, the air was humid and the sky cloudy, the earth would have been much moister.

It is necessary, therefore, to take into consideration such complex meteorological factors as the rainfall, winds, and temperature, in order to obtain an exact idea of the relations which exist between meteorology and the dampness of the soil. And it will be necessary especially to consider the correlation between the rainfall and the level of that subterraneous water which we know has so much importance in the local production of malaria. What is the radius of influence of the rains on this subterraneous water? How long after is this influence felt? Have the local rains any influence on it? How and when do the distant rains influence it?

Perhaps it will be necessary to take into consideration also that very notable meteorological phenomenon of the dew here in the Campagna.

Other correlations are also admitted to exist between the rainfall and malaria. Thus it has been maintained that the *autumn rains*, when they are abundant and cold, arrest or put an end sometimes rather quickly to the æstivo-autumnal epidemy. Certainly they destroy many of the mosquitoes, and a sudden lowering of the thermometer coincides with the sudden diminution of the primary fevers. It is also admitted generally that a downpour in the summer is quickly followed by an outbreak of fevers; this has been explained by referring it to the causes predisposing to chill. But this relation between the *summer rains* and malaria is not in the least supported by Santori's observations.

Tacchini, in the above-mentioned years (see page 159), has also contrasted the *scirocco* days (that wind which was believed to be the carrier of malaria) with the percentage of the fevers. But, as Table XIII. demonstrates, in 1878 there was, in the same epidemic period, that is, in the third quarter of the year, the maximum of *scirocco* days and the minimum of malaria. Neither is there any correlation between the nebulosity, nor between the blowing of the *tramontana*, and the course of the fevers.

Therefore, for the moment, the correlations between meteorology and malaria are not very marked. It is desirable, however, that all these data should be coordinated in such a way as to enable one to discover the correlation which certainly must exist.

With this intention we, at the farm of Cervelletta, an intensely malarious place, have taken daily notes of the individual cases of fevers, recording the results of microscopical examination of the blood, the life and habits of the mosquitoes, the meteorological data, and the work and life of the *campagnoli*.

In June and the early days of July, that is, between the end of the old and the beginning of the new epidemic year, we found, as we have said, the quartan recurrences prevalent, less frequently the tertian, and much less frequently still the mild summer fevers.

With the new epidemic year this order of things is reversed, that is, the summer fevers prevail, but the cases of mild tertians are less in number, and the quartans are slow in appearing.

The course of the epidemy in this year is given in

TABLE XV.—PRIMARY CASES OF MALARIA AT CERVELLETTA OCCURRING DURING THE SECOND HALF OF 1899

	July	Aug.	Sept.	Oct.	Nov.	Dec.
Æstivo-autumnal Fevers	10	30	15	7	3	1
Mild Tertian . .	3	7	3	2	1	1
Quartan . .	—	1	1	3	2	3

Consequently the quartan has a special epidemic course, inasmuch as it is the last to begin and, as we have seen, the last to recur, and it reaches its maximum when the other fevers fall to their minimum; all this corresponds with the fact that in some tropical regions this form of malaria is very rare, or is altogether absent. The mild tertian and the æstivo-autumnal fevers, on the contrary, have a similar but not identical course, since in the years and places of severe malaria the latter are notably in excess of the former. The reverse also probably takes place in the years and places of mild malaria.

In individuals who inhabit, especially for a long time, an unhealthy locality, it is not difficult to meet with, either contemporaneously, or one after the other, double malarial infections, that is, caused by two species of parasites. It is rare to meet with triple infections. And since the æstivo-autumnal fevers are always the first to become rare in their recurrences, one readily understands why in spring those fevers which Marchiafava and I, *a potiori*, called spring fevers, that is, mild tertian and quartan, are prevalent with us.

At the commencement of the epidemic time of the year, malaria being very frequently a domestic disease, it is easy to see that the first cases of new mild or severe tertian infections occur in the houses or huts where the last recurrences of these fevers are found.

It is remarkable that after the very first cases there was a truce of 17–18 days, after which the epidemy spread.

The life of the *Anopheles* mosquitoes has a direct and intimate relation with the general epidemic course of the malarial fevers.

We found, after hibernating during the winter the larvæ in April became transformed into nymphæ, and then into mosquitoes. In the first half of May the new generations of larvæ made their appearance in some waters; they were more common in June, and in the second half of this month they

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appeared in the rice-fields, where they increased from day to day by successive generations; in July and August, besides having increased in the rice-fields, they were found in all the clear and slowly running watercourses; here they remained till the abundant autumn rains washed out, so to speak, and cleansed the watercourses; and at the end of the year they were found only in the rice-fields and in the deeper collections of waters.

The mature mosquitoes, in their turn, were still rather easily found during March in grottoes, huts, and stalls; in the huts some of them were full of blood. In April and May they were very scarce in these places and were no longer full of blood. In the first half of June they reappeared in considerable numbers in the grottoes and huts; in the second half of this month they were more numerous and had begun to bite; in the huts the females were more numerous, and were full of blood, in the grottoes the males were found, but always without blood. Towards the end of June we found the first infected *Anopheles*, and these increased in number during July, August, and September. After the autumn rains they diminished greatly in number, and when the cold weather appeared we found them as usual hibernating in the stalls and houses.

Therefore, the correlation between the malarial epidemy and the life of the *Anopheles* mosquitoes is very evident, and now more than ever is it necessary to study in malarious places the season of the malarial mosquitoes, and to investigate its course and variations. Here must rest the ultimate cause of the periodic course of this disease, and of its diverse annual course in various climates.

If we analyse briefly this correlation for each of the three principal types of the fevers, we find, setting aside the hypothesis that one species of the parasite can transform itself in the body of the mosquito into another species by the influence of external conditions: setting aside also the other hypothesis, which, we have seen, cannot be accepted, namely, the hereditary transmission of the malarial infection from infected mothers to the young mosquitoes; that to explain the appearance of the epidemy of the summer fevers there remain only these two hypotheses:

Either the first cases of these fevers in July are recurrences of a previous infection, as was observed last year at the farm of Rustica;

Or the very first cases of these fevers in July are primary, as was the case at the farm of Cervelletta.

Both hypotheses are possible. In both we have to deal with a contagion, circulating, so to speak, between the temporary host (man) and the definitive host (mosquito), a contagion which, by means of the blood of the relapsing cases of the preceding year, is transmitted by the agency of mosquitoes, and starts the epidemic of the following year.

This transmission of the contagion as regards the mild tertian is very manifest. We have had a good example of it at the farm of Torsapienza, where for the whole of the second quarter of the year there were only cases of mild tertian, and when the summer epidemic appeared it continued to be of the same type of fevers.

Nevertheless, it still remains to be explained why the summer fevers so notably predominate in neighbouring places, as at Cervelletta; and why sometimes there is an interval, sometimes a long one, between the last appearance of gametes in the blood of the relapsing cases and the first appearance of asexual forms of the primary fevers; and why the quartan appears and develops last. Is this last fact due to a longer period of incubation, or to its hæmosporidia having to await their development till the first fall of the temperature which is produced by the summer or autumn storms?

To decide all these and similar questions it will be necessary to continue for years comparative and systematic research like that which has been carried on for a year at Cervelletta. For the present we can only say, speaking generally, that intimate relations which are not yet thoroughly defined, must exist between the temperature and the development of the various hæmosporidia of man in the body of the malarial mosquitoes, both outside and inside habitations.

I would add, in explanation of this epidemy, that from July onwards there also enters into consideration the predisposing causes of social origin, these being able to revive some recurrences after long intervals of the æstivo-autumnal and spring fevers, and being able likewise to concur in facilitating the new infections of the mosquitoes and of man. And now, to bring to a close this first part on the epidemiology of malaria, it is time to speak of the

SOCIAL CAUSES OF PREDISPOSITION OR OF IMMUNITY.

These are multiple, inasmuch as they embrace that very important *ensemble* of causes which arise from the position of man in his social environment, or from his economic conditions, or from the class to which he belongs.

Unfortunately on the human race there still weighs that fate by which both preventible diseases and premature deaths, as well as the duration of life itself, essentially depend on economic institutions.

Malaria is not an exception to this sad rule; on the contrary, it is a painfully manifest example of it. We shall therefore briefly analyse these social or economic causes of predisposition to and of immunity against the epidemy of malaria, which are: alimentation, housing, clothing, work, and education.

Alimentation.—It is certain that food should always be proportionate to the amount of work performed. Well, we shall see what in reality is the diet of the peasant who works in the Agro Romano. As the type, we can take the diet of the Abruzzese peasant in the Roman Campagna, as shown in Table XVI. The ration of this poor pariah for a great part of the year, that is, except at harvest time, consists exclusively of maize of varying qualities.

Dr. Memmo has calculated by direct experiments the nutritive substances introduced and assimilated, in the form of polenta, polenta cake, or bread, the percentage of loss with the fæces, both of the total ration and of the azotised substances, and the balance of the *calorie*.

When his figures are compared with those of the ordinary average workman of Voit, we find the nutrition of our peasant is deficient in albuminoid substances, while it has, on the other hand, an excess of carbohydrates, which makes it passable; it is true, calculating it in *calorie*, it exceeds that of the above-mentioned workman, a surplus which, however, is much reduced and becomes a *deficit* whenever the work gets fatiguing or excessive.

TABLE XVI.—ALIMENTATION OF THE ABRUZZESE PEASANT IN THE ROMAN CAMPAGNA.

	Daily ration in grams of nutritive substances						Loss with the fæces %		Balance of the calorie		
	Introduced			Assimilated							
	Albuminates	Fats	Carbohydrates	Albuminates	Fats	Carbohydrates	Total ration	Azotised substances	Total	Per kgr. of weight of the body	Per Sq. M. of surface
Maize, third quality	61	43	805	43	36	761	8	30	3629	57	1822
„ first „	88	50	773	72	43	731	7	18	3691	58	1853
Ordinary average workman of Voit	118	56	500	105	—	—	—	12	2868	40	1399

The defect, then, of the azotised substances manifests itself in the inexorable and lasting physical and moral injuries which give rise to the starved appearance of our poor peasants and in his predisposition to malaria and other infectious diseases.

The shepherd in the Campagna who gets, as his right, a daily ration of wheat bread, and sometimes milk, works much less, is much better fed, and consequently more healthy, than our peasant who eats bread only, and not that always, on the days of excessive work, that is, when mowing the grass, and reaping and threshing the corn.

It happens that this poor pariah, who works for others infinitely more than for himself, is frequently the slave of his masters, not always humane nor disposed to give him sound maize, and he is nearly always the slave of the so-called *caporali* (overseers), who cut off his wages and food with impunity, or give him the latter in insufficient quantity and sometimes even diseased; at any rate they make him pay a high price for it. Under the most favourable circumstances, there being no means of readily procuring food in the Campagna, he must buy it at the so-called *dispense* (stores) belonging to the farms, where, in the absence of all competition, the storekeeper or the master has absolute power.

We add finally that from 1700 onwards the daily wage here in the Campagna has increased only 50 %, while the price of food has more than doubled: so that to-day the conditions of life, especially as regards food, are much worse, notwithstanding the increased profits from the land. According to Sombart, if a hundred years ago the gross profit of a farm was equal to 100, the labourer received thirty parts of it, and thirty-five formed the clear profit of the owner; to-day the gross profit is equal to 200, and while the owner takes 130 parts, the labourer receives barely thirty parts as in the past.

Housing.—Malaria being very frequently a domestic disease, one understands the great importance of this factor in relation to epidemics of the disease.

The most common type of habitation in our malarious places is certainly the hut, of an oblong or round form, terminating in a ridge above, made of straw, maize canes, and wild plants, with the floor somewhat sloping, and surrounded outside by a trench for the discharge of the water.

Popular tradition has taught the peasants to place these huts on the highest and best ventilated hills, in accordance with what we have said about the wind which disperses and does not carry malaria.

There are two principal types of these huts. One, the more rare, and used as a habitation for several families, is a kind of long arched corridor, with a door at either extremity; in the interior along both sides are placed the benches for sleeping on, in one, or sometimes in two tiers. The beds are made from the trunks of trees, covered with straw, a mattress made of maize leaves, and a few rags for covering. In the middle of the floor is a line of fireplaces for the different families. The smoke given off by the fires, filling the hut, acts, as we shall see, as a prophylactic against malaria, by driving away the mosquitoes; in all other respects this hut resembles that of primitive man. The other type, much more common, consists of many small huts, each for one family, but in all other respects similar to the former. Figure 31 represents a collection like a village of these characteristic habitations of our Campagna, situated along a road which terminates at one of those mediæval towers raised for defence against the Saracens (see page 8); fig. 32 shows one of them, with the people who inhabit it round about.

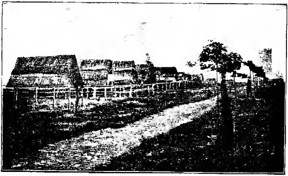

FIG. 31.

Many other poor people are, if possible, housed even worse. In 1875 Dr. Balestra described in vivid colours the miseries of our *campagnoli*, and vainly appealed to the sympathy of the rich landlords and tenants. Vitelleschi, in his report to the Council for the Agrarian Inquiry in 1883, protested in vain that here, near the seat of one of the most ancient centres of civilisation, at the gates of the capital, a spectacle presents itself much more painful than that of man who lives in savage habitations. In 1881, for a more or less stable population of 12,734 persons there were only 556 houses in the Campagna. And when the unfortunate ones, driven by the cold and hunger from the mountains to the plain, meet with some old house or broken-down building, they take refuge in it, huddled together without distinction of sex or age, and without any of the comforts almost indispensable to human life. And these, adds Vitelleschi, are not the most unfortunate, inasmuch as many others, not finding a building of any kind, live as modern troglodytes in grottoes excavated in the tufaceous hills. Many of these inhabited grottoes (see fig. 33) are to be seen in the Campagna; the census of 1881 gives 469 of them!

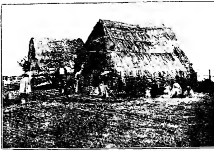

FIG. 32

Again in the summer, that is, in the months most dangerous for the fevers, during the hay-making and reaping, when the casual workers come in thousands, nearly all are obliged to sleep in the open air under a piece of stuff supported by four poles; a few take shelter in small and unsuitable premises, where they are frequently so overcrowded that a hundred persons are made to sleep on

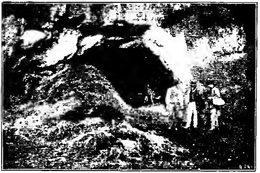

FIG. 33

boards supported on trestles in a room large enough for ten, just like poor emigrants in emigrant ships.

The houses, besides being scarce, are generally constructed without any special prophylactic precautions against malaria, except that frequently, when possible, they are placed on high ground. Some of the mediæval cottages are, as we have already said, built upon ancient monuments along the ancient ways.

The surface of the Campagna varying much in character, and malaria being, as we have said, autochthonous, it is not surprising that fairly inhabitable places exist here and there. Some of these were, as we have seen, famous in ancient times (see page 4), but they were afterwards abandoned. Others, such as Laurentum and Veii, were transformed into mediæval *domocultæ* (see page 6), to which new ones were added in the more healthy localities, which gradually became the modern communities of Anzio. Castelnuovo di Porto, Formello and Campagnano. Later, other inhabited centres such as the Castelli Romani were established in the hills above the Campagna. Similarly, all the villages and towns in the whole malarious zone of the province of Rome were built on hills in order to protect them from the underlying malaria.

It is notable that in these towns malaria frequently prevails in the houses which face the unhealthy quarter.

It is also notable that sometimes sporadic cases, so to speak, or distinctly domestic epidemics, occur in houses situated in healthy places, but put into communication with a malarious district by means of the hay-carts and closed carriages which travel between the two places; this fact, for instance, has been verified at Velletri, in the house, situated in a healthy locality, where the diligences from the Pontine Marshes stop.

In the same way, malaria may be contracted or be transported to a distance in a railway-carriage, when it contains an infected mosquito.

The origin of the ship epidemies must also be similar; they should, however, as we have said, be more carefully investigated by means of the more modern methods of diagnosis and from the new epidemiological standpoint.

Clothing.—The miserable peasant of the Campagna is generally so insufficiently and badly clothed that he is not protected from chills, to which he is so liable in the Campagna, nor from the bites of insects. The poor people, and especially the children who swarm in the huts, are frequently seen in an almost nude condition; hence, perhaps, the heavy tribute they pay to malaria.

Work.—In May and the early part of June, the very fatiguing work of mowing and hay-making begins; this is performed by casual labourers who come mostly from the Marche, and this being, as we have said, the healthiest season, it is very rarely that when they return to their homes they take with them the malarial infection, notwithstanding that they work for seventeen or eighteen hours a day with only two short rests.

Then in June comes a still more fatiguing work, that of reaping, which is generally done by other labourers, also casual, who come from the neighbouring villages, such as Rieti, Frosinone, Teramo, and Chieti. This work, in respect to malaria, is more dangerous than the former, especially in some years.

With July and August comes the period of excessive labour—namely, threshing the corn. When the corn has been gathered, there remain or come from other places a certain number of men for the threshing, which is generally done by machines; but it is nevertheless very fatiguing working in the hot sun all day, and being exposed to the cold and damp of the night and early morning. In the night these poor people sleep in the open air, beside the machines, or at best under a hut made of the green branches of trees, and consequently they are exposed continuously to the bites of mosquitoes, which may carry the contagion from one person to another. They light fires, it is true, with the idea of killing the mosquitoes that collect there, but these fires kill very few or none of the large number of those which they attract.

This excessive work lasts, with short rests, for some, such as the feeders, from before sunrise to the evening, and for those who attend to the machines from the rising to the setting of the sun; for others—that is, those who attend to the corn—it lasts during the whole day, every alternate four hours, and is performed by people who are exposed to very great changes of temperature, and who live on the food we have described. Therefore this excessive work helps to explain, as an additional predisposing cause, the recurrence of the fevers, and consequently the infection of new mosquitoes; it also explains the appearance of the epidemy in July, and its greatest prevalence in August. And consequently it will be important to ascertain if there be any correlation between the longer or shorter duration of this work (according to the variations of the harvests in different years) and the annual number of cases of fevers.

When the harvest is finished, the Campagna fortunately becomes depopulated.

From the latter half of September onwards the peasants, who live here for several months in the year as settlers, descend from the mountains again for the maize harvest; this is not very laborious work, but it is dangerous as regards malaria, especially in those years when the heat is prolonged, and thus also the fever season.

The shepherds also with their flocks descend from the Central Apennines in the latter half of September. They are fortunate enough to migrate from the Campagna in June, before the fever season begins, and to remain away in an excellent climate during the months malaria is most prevalent in the Campagna.

The people who work in the woods arrive in November and leave in April or May; so that, though they live in these woods like the inhabitants of virgin forests, they generally avoid contracting the disease. And the same happens fortunately with the so-called *aquilari*, that is, the workmen who from November to May are employed in irrigation work.

These, as all the other peasants of the Campagna, except the shepherds, are subject to the tyranny of the sweaters, who go under the name of *caporali*.

In olden times it was the custom, in order to afford opportunities for improvements, for the rents to be paid at long intervals, and for the workers to contract directly with the agent or the proprietor of the land, while to-day all contracts, with very few exceptions, are made through the *caporale*, whose power is as absolute as it is unjust.

He puts whole families of workers in his absolute power, while they are still in the mountains, by advancing small sums of money to them. When he has collected together the number of *braccia* that he requires for a given work in the Campagna, he proceeds to divide them into three categories: one consisting of the strongest men; another, called *bastarda*, of women and men, less able to work; and the third, that of the *monelli*, of women, old men, and children. The hardships to which these unfortunate people are exposed in their march on foot, in cars, or in railway-carriages, the ill-treatment, sometimes even corporal, to which they are subjected, complete the series of their miseries, that New Italy, entering Rome in 1870, has not only failed to relieve, but has done a good deal to increase. It is shameful to see here at the gates of the capital how this form of tyranny is maintained and thrives with impunity, by which the miserable peasant, who through hunger migrates from his mountains to obtain work, is humbled like a slave, and treated worse than a dog. And it is grievous to see how, for their convenience, to save themselves the trouble of dealing directly, as all the employers of every civilised country do, with the workers, our rich leaseholders and landlords permit such a condition of things to continue which, besides being contrary to all the usages of the most rudimentary civilisation, strongly predisposes to the spread of malaria.

Finally, among the causes of social predisposition must also be included

Education.—When this, on account of poverty, is wanting, all the most injurious prejudices, both regarding the sources and vehicles of the infection, and as to the mode of preserving oneself from it and of treating its sad effects, arise and persist.

Fortunately traditional experience in malarious places has taught and teaches many useful prophylactic rules: and the new theories on the transmission of the fevers by the agency of mosquitoes find more ready acceptance among the people than among the half-cultured and the doctors themselves. Nowadays the old prejudices against quinine, and the mode of taking it, have almost disappeared. But the misfortune is that this remedy is not easily obtainable, nor is it as cheap as it might be. And medical assistance, owing to the great distances and to the imperfect means of communication, is very insufficient, and unprovided with the means of succour even where and when it is most required.

PART II.

PROPHYLAXIS.

MEANS DIRECTED AGAINST THE INFECTIVE CAUSE.

(A) For Destroying the Malarial Germs.

Verification of the Diagnosis.—The first step towards a good and rational prophylaxis is, as usual, the diagnosis of the disease, there being other morbid processes which simulate the malarial infection.

For making the diagnosis, the *examination of the blood*, which may be made in the fresh state or by staining, is necessary.

For *the examination of the fresh preparation*, to avoid pain, the lobe of the ear is pricked with a needle, and a very thin stratum of blood is made by pressing in a pocket-handkerchief the cover-slip against the slide. Considerable practice is however necessary, especially for recognising the non-pigmented or slightly pigmented amœbulæ of æstivo-autumnal infections; these are frequently confounded with the vacuoles in the red corpuscles, which have nothing to do with the parasites.

This examination, if made by an experienced person, not only enables him to make the diagnosis of malaria at once, but also reveals to him the clinical variety of the fever, and the stage of the febrile period, particularly if the attack is about to begin; and this with such precision that he frequently can correct the anamnesis obtained from the patient. This microscopical examination is also useful as an aid to prognosis and treatment. In fact, there are grave cases of coma, in the presence of which even the most able clinician may remain perplexed; but one droplet of blood will demonstrate at once whether the case is one of pernicious fever or not, and will enable us to undertake specific treatment with energy and promptness.

One has recourse to the examination of *stained preparations*, especially when the blood collected cannot be examined within half an hour or an hour at most, and when one has not had much practice in examining fresh preparations. For this purpose the cover-slip must be thoroughly cleansed; the lobe of the ear, or the tip of the finger, to be pricked, is thoroughly cleansed with alcohol or ether. It is necessary to spread out a very thin stratum of blood on each cover-slip, leaving it for some minutes to dry in the air, and then the cover-slips are placed in absolute alcohol, to fix the blood corpuscles and the parasites. After fifteen to twenty minutes the cover-slips are dried, and are then ready for staining, which may be done at one's convenience even months after.

There are several methods of staining: there is first our simple method of staining with methylene blue, which acts better, as Guarnieri and I have demonstrated, if the stain be dissolved in blood serum or in ascitic liquid; and there are the double staining methods. These are done with various stains; but the best method is that described by Ehrlich in 1889, modified in 1891 by the Russian physician Romanowsky, and improved by Ziemann in 1898. The staining fluid is a mixture of a solution of eosin with a solution of methylene blue, which develops a third stain, that colours the chromatin. So that in reality it is triple staining. The eosin stains the red corpuscles pink, the methylene blue stains the hæmosporidia blue. The third stain colours the chromatin, which, as we have said, plays such an important part in the structure and reproduction of the parasites, a kind of violet tint.

The proportions of both solutions are as follows:—

TABLE XVII.

(A) *Very pure medicinal methylene blue* (Meister Lucius).—Saturated watery solution kept for three days at 25° to 30° C.

(B) *Eosin A, G, or B* (Meister Lucius).—Watery solution, 1 %.

Take of A—parts 1–3.
" " B—parts 2–5 and mix.

The mixture must act on the preparations from 20 to 30 minutes.

We cannot indicate in every case fixed proportions of the two solutions, because, no matter how slightly the conditions vary, the proportions necessary for obtaining the third stain at once alter. One frequently has to make several trials, keeping between 2–5 parts of eosin and 1–3 parts of methylene blue. And often, in spite of every care, we obtain an imperfect staining, or a precipitation of needle-shaped crystals which prevents a proper examination of the preparation being made.

The cover-slips with the blood are placed separately in a little vessel full of the staining mixture. The staining completed, they are washed repeatedly in distilled water, dried slowly with the flame, and mounted in Canada balsam.

Isolation.—This is the first prophylactic measure, which should be adopted directly the diagnosis has been verified. In a malarious place, whoever is affected with the seasonal fevers is dangerous to others, and consequently should be isolated. Malaria, since the latest researches, must no longer be considered a miasmatic disease, but a typically contagious disease, that is, a contagion which is transmitted from man to man, not directly, but by the agency of the mosquito.

The malarial patient, then, should be removed immediately from the place where he has acquired the infection, and, as much for himself as for others, should be ordered the *fuge cœlum in quo ægrotasti*: for himself, he being exposed to fresh bites of infected mosquitoes, and therefore to new infections of the same or of other malarial parasites, as occurs in mixed infections; for others, because the sexual forms of the parasite are the source of infection to mosquitoes, and consequently to man. It is for this reason, for example, that the Roman hospitals, in regard to the malaria of the Agro Romano, are not only places for treatment but also for isolation. In fact, in

Rome proper that carrier of contagion, the malarial mosquito, does not exist.

We have seen that the forms of the parasite which complete in this insect their cycle of sexual life are those extraglobular forms which to-day we more appropriately call gametes, and which, as we have already seen, belong to the endoglobular phase which terminates with the free life in the plasma. They do not appear so much in the circulating blood during the primary attacks of fever, as after the subsequent attacks, and there they remain for a long time, sometimes for months, especially in the æstivo-autumnal fevers. Therefore it is not only in the first acute period, so to speak, of the infection that the patient is dangerous to others, but also during the whole time of convalescence, which is often prolonged. And a truly rational prophylaxis of malaria will be possible only when sanatoria are instituted where the convalescents can be retained until by repeated examination of the blood, and perhaps also of the spleen, the absence of the free forms or gametes has been verified. If later on, as is probable, a way be found of preventing with culicifugal substances the biting of malarial individuals by mosquitoes, then this isolation will be much facilitated, and it will be possible to obtain it without the removal of the patient, by placing some protective material on the exposed parts of the body, or any of the substances that drive away mosquitoes, and consequently prevent the bites of these insects, which are the propagators of the infection.

Disinfectants.—These must attack both the sources and the carriers of infection.

The disinfection of the infective source, when it is in man, consists altogether in the *disinfection of the blood*. The specific treatment is a true internal disinfection; quinine is the specific disinfecting substance of malarial blood.

This drug was introduced into therapy in olden times. The Countess del Chinchon, wife of the then Viceroy of Peru, suffered from malarial fever in 1638 at Lima, and by the advice of the Supreme Judge of the place tried powdered Peruvian bark, which was popular there as a remedy for this disease. Her physicians were opposed to it, saying that it savoured of witchcraft. Wherefore the superior of the Jesuit convent intervened and blessed the powder, and the Countess, who took it, was cured as if by magic. The remedy was afterwards introduced into Europe under the name of Cinchona bark, or Jesuits' bark, after the Jesuit fathers who advised its use. Its success quickly became known. Nevertheless, thirty-two years after, Cardinal di Lugo, at Rome, had to protect its sale with a decree, by which it became known as the Cardinal's powder. And forty-five years later, Charles II. of England, owing to the opposition of his physicians, had to take this drug secretly for malarial fever; having been cured of it, he made a decree guaranteeing and protecting Talbot, the inventor of the tincture of bark which had cured him. The medical faculty at first was diffident in accepting this remedy, though its value was recognised by such able men as Sydenham and Torti. The latter, who obtained such splendid therapeutic results, even in the severe forms of malaria, was accused by his colleagues of causing the death of the pernicious cases of malaria with this treatment.

Great therapeutic progress was made in 1820, when the alkaloid was extracted from the crude bark by the French chemists Pelletier and Caventou.

In order to make a thorough disinfection of the malarial blood it is very advisable to study the action of this drug, so that one may be able to know the manner and the time in which it should be administered.

In 1869 the pharmacologist Binz made some admirable studies on this subject. He had a truly prophetic instinct; he divined that the cause of malaria was a protozoon, an amœboid organism, because quinine, so efficacious against malaria, has a specific action on amœboid organisms, suddenly arresting their movement.

And, indeed, this has been verified. Under the microscope Marchiafava and I saw that, on adding a trace of a solution of quinine, the hæmosporidia, which previously exhibited active amœboid movements. became still, and were expelled from the red corpuscle.

So that the action quinine has on the malarial parasite tends to confirm the fact that it is a protozoal organism. This, moreover, was one of the arguments that Marchiafava and I brought forward in 1885 in favour of the new etiological theory of malaria. The action of this remedy is, however, not yet fully understood.

Lo Monaco and Panichi have recently seen that on introducing a solution of quinine into a fresh preparation of malarial blood, the endoglobular parasites under the microscope feel its influence. This, however, is manifested differently according to the strength of the solution of quinine used. Thus very weak solutions cause the parasite to swell; weak solutions stimulate it for a short time; those of medium strength stimulate the parasites markedly and terminate in the extrusion of the parasite from the red corpuscle: finally, strong solutions cause the parasite suddenly to contract within the corpuscle.

They have also observed that the resistance of the parasite to the action of quinine is not always the same, inasmuch as it is diminished at the approach of the febrile attack and during its development, while the resistance reaches its maximum degree during the period of apyrexia.

On the basis of these results the authors have been able to determine the rational dose of quinine necessary for the cure of the malarial infection, and to demonstrate that if quinine does not act so promptly on the summer and quartan forms of the parasite as on the mild tertian form, this depends on the greater resistance which the young forms oppose to the specific remedy.

Nevertheless, the mode of action of quinine is not so simple. It appears that it also has a necrotic action on the protoplasm of the parasites. In fact, by the Romanowsky method of staining, one sees, after a malarial patient has been subjected to the action of quinine, an alteration in the protoplasm of the parasite, especially in the chromatin, which is no longer seen, or is very scanty. Perhaps the quinine acts by combining with the protoplasm and that this action takes place even through the red corpuscle, but we do not know in what way the latter participates in it.

What is the proper time to give quinine to a patient suffering from malaria?

Sydenham said that it should be given after the attack, while Torti suggested giving it before the attack.

In reality, quinine, when given in a sufficient dose —namely, 2 grammes of the sulphate or bisulphate— has always a good effect; moreover, in severe fevers one must not wait to give it at this or that particular moment, but should give it immediately, if necessary even by the subcutaneous injection of the dihydrochloride, and continue to administer it in divided doses up to 1–2 grammes a day. But when one can wait to study carefully the rhythm and the precise hour of the febrile invasion, it can be given according to either Torti's or Sydenham's precepts. In the first case—namely, that in which quinine is given a little before the attack—this will supervene just the same, sometimes, however, in a milder form, at other times without being weakened in the least. Nevertheless, another paroxysm will not occur, or if it does, it will be milder; and if a large dose of quinine be given before this second attack is due, very probably it will not occur, and almost certainly the third paroxysm will be cut off.

On the other hand, if the quinine be given when the attack is ending, that is, in the sweating stage, which is the time when there are the greatest number of young amœboid forms in the circulating blood, it will prevent the recurrence of another paroxysm. Consequently, if one can wait, this is a suitable time for administering quinine. At this time the stomach tolerates it better, and there are in the red corpuscles young amœbulæ endowed with amœboid movement, which is arrested by the alkaloid. A little before the attack begins, when the gymnospores are in the circulating blood, the quinine is but slightly efficacious against them. It also has little effect on the parasitic forms which give rise to the obstinate recurrent fevers.

Practising last year in the Campagna, we have seen cases of recurrent fevers in persons who had regularly taken quinine immediately after the very first attacks, in a daily dose of 2 grammes for 4 days, 1 gramme for 4 days more, and then 2 grammes every 6 days.

Still more, unfortunately, quinine does not act on the gametes that ensure the sexual cycle in the mosquitoes; even when giving quinine every day by subcutaneous injection and in large doses for a whole month, I have not often succeeded in destroying the crescentic forms. Thus, after the administration of the drug, even the gametes of the tertian and quartan continue to circulate in the blood.

Upon these forms of the parasite, which are the most dangerous from the epidemic point of view, quinine has no influence.

In fact, by making *Anopheles* bite men undergoing quinine treatment and having crescents in their circulating blood, the sexual cycle develops in spite of the treatment. Consequently complete disinfection of malarial blood cannot always be obtained, and therefore a complete rational prophylaxis by means of this disinfection, notwithstanding what Koch says about it, is not easy, nor is it always possible.

Fortunately it is known that, by giving quinine to malarial patients at the beginning of the fevers, one can generally prevent or notably reduce the formation of the gametes.

Therefore, by the employment of an early and well-continued specific treatment, we can and ought to prevent as much as possible the development of the forms destined to transmit the infection from man to man, through the mosquitoes.

Unfortunately for the carrying out of this disinfection of the blood, the difficulties are not few among the poor people of the Campagna, who remain in the place where they have been infected and during the favourable season continue to be reinfected. And not rarely cases of intolerance of quinine are met with.

Consequently it is more than ever necessary that sanatoria should be built in healthy and elevated sites for the reception of at least the most severe cases of malaria from the first paroxysms of the fever till their complete cure.

We now proceed to consider the *disinfection of the source, and at the same time the carrier of infection—the malarial mosquito.*

This is a disinfection *sui generis*, which, even before it was known how dangerous some mosquitoes were, has been attempted, in order to prevent or lessen the great discomfort which the bites of these insects produce in man.

Mosquitoes can be destroyed in various ways, according to the two periods of their life—namely, the aquatic and the aërial. And even during the aquatic stage of their existence, their powers of resistance differ; thus, the eggs are moderately resistent; the young larvæ possess very little power of resistance; whereas the adult larvæ, and particularly the nymphæ, are very resistent.

Fortunately for the practical employment of disinfection, the nymphal period is transitory, and is very short in comparison with the larval stage.

The problem consists, therefore, in practice, in destroying the larvæ in the water and the mosquitoes in the air.

For this purpose Dr. Casagrandi and I have entered upon a long investigation, the first results of which are shown in the following tables, where the substances used, their strength, and the maximum time they take to kill the larvæ and nymphæ of mosquitoes are tabulated.

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Destruction of the larvæ.—Attempts at the destruction of the larvæ have been already made elsewhere. In America there are regions where no one can live on account of mosquitoes; so much is this the case that prizes have been offered to any one who finds the most practical means for destroying them.

They have had recourse to the breeding of fishes in ponds, hoping that these would destroy the larvæ; but it did not prove successful—as was to be expected, because there are examples of various malarious regions in which the larvæ abound in ponds that have been used for breeding fish. It has been proposed also to rear in ponds and other collections of water dragon-flies, knowing that both the larvæ and imagoes of this insect are carnivorous, that is to say, the larvæ of the dragon-flies destroy the larvæ of the mosquitoes and the dragon-flies the mosquitoes. But even this means is unsuccessful, inasmuch as mosquitoes are so prolific that they can be destroyed only to a small extent by dragon-flies.

A remedy, which was also proposed in America, and which acts much better, is, as we shall see, petroleum.

Table XVIII. shows the substances which act on the larvæ of mosquitoes.

From it we see that the vegetable kingdom supplies some very energetic larvicidal substances: for example, infusion of tobacco leaves, and powdered unexpanded flowers of Dalmatian chrysanthemums or pyrethrums (*Chrysanthemum; Pyrethrum cinerariæ-*

folium), which are the essential part of the so-called insecticide powders, and are potent specific poisons, killing the larvæ in a few hours.

TABLE XVIII.—ACTION OF CULICIDAL SUBSTANCES ON THE LARVÆ OF MOSQUITOES (C. PIPIENS, C. ANNULATUS).

At the Ordinary Temperature (18° to 20° C.).

Number	Substances employed	Maximum time required to kill the larvæ
		Hours
1	Tobacco leaves, saturated watery infusion of	3
2	Potash $^0/_{00}$	4
3	Chrysanthemum powder (unexpanded flowers) 0·03 $^0/_{00}$	7
4	Corrosive sublimate 1 $^0/_{00}$	10
5	Chrysanthemum powder (2nd quality) 0·06 $^0/_{00}$	12
6	Sulphurous water, non-saturated	12
7	Salt water (5–10 $^0/_{00}$ NaCl)	15
8	Extract of tobacco of commerce at 10 $^0/_{00}$	20
9	Bisulphites of soda and of potash 1 $^0/_0$	20
10	Sulphate of copper 1 $^0/_0$	24
11	Sulphate of iron 1 $^0/_0$	24
12	Tar 10 $^0/_0$	30
13	Ammoniacal water of coal-gas	45
14	Milk of lime 5 $^0/_0$	48
15	Sulphuric acid 1 $^0/_{00}$	48
16	Potassium bichromate 2 + H^2SO^4 3–1 $^0/_{00}$	48
17	Valerian root, saturated watery infusion of	72
18	Quassia amara	72
19	Solanum nigrum	72
20	Daphne Gnidium	72
21	Sodium sulphite, saturated watery solution of	72
22	Potassium permanganate 5 $^0/_{00}$	72

Among the mineral substances potash in normal tenth solution or a little stronger also acts quickly. Corrosive sublimate, which is such an energetic bacterial disinfectant, is in this case not very active, requiring at least five hours to kill the larvæ, even in a solution of 1 $^0/_{00}$, while the nymphæ live for a longer time. Sulphurous water, even non-saturated, and salt water 5 to 10 % are also sufficiently energetic larvicides.

Next come a series of substances that act less energetically, from the bisulphites to permanganate of potash, which, even in solution of 5 $^{0}/_{00}$, does not kill the larvæ until after three days, and consequently, for this reason, as well as owing to its cost, is not practical. Moreover, in marshy waters, where there is so much organic material, it would lose a great part of its action.

It is interesting to see separately the larvicidal efficacy of certain staining substances derived from coal tar.

TABLE XIX.—CULICIDAL ACTION OF ANILINE DYES ON THE LARVÆ OF MOSQUITOES (GEN. CULEX).

Number	Aniline Dyes	Proportion per mille	Maximum time required to kill the larvæ
1	Green malachite	0·50	6^{h}–12^{h}
		0·025	24^{h}–26^{h}
		0·0125	34^{h}–48^{h}
		0·0062	36^{h}–108^{h}
		0·0031	48^{h}–survive
		0·0015	survive
		0·0007	"
2	Gallol	0·50	6^{h}–12^{h}
		0·025	16^{h}–24^{h}
		0·0125	24^{h}–36^{h}
		0·0062	30^{h}–72^{h}
		0·0031	36^{h}–72^{h}
		0·0015	48^{h}–108^{h}
		0·0007	72^{h}–survive
3	Larvicide	0·50	2^{h}
		0·025	2^{h}, 45
		0·125	4^{h}
		0·0062	5^{h}
		0·0031	6^{h}
		0·00125	7^{h}
		0·00062	9^{h}
		0·00031	16^{h}
		0·00015	24^{h}
		0·0007	48^{h}
		0.00031	72^{h}

These results enable us to conclude that among the *aniline dyes* (blue, violet, red, yellow, green), those which have the most energetic action are larvicide, gallol, and green malachite A.

Of these three colours the most active is larvicide, whose certain larvicidal dose in twenty-four hours is 0·00015 $^0/_{00}$, while for gallol it is 0·0125 $^0/_{00}$, and for green malachite A 0·025 $^0/_{00}$.

The minimum larvicidal dose of the first falls to 0·000031 $^0/_{00}$, while for the second it stops at 0·0007 $^0/_{00}$, and for the third at 0·0031 $^0/_{00}$.

The two best larvicidal substances, larvicide and gallol, are supplied by Weiler-ter-Meer, of Uerdingen, and the green malachite A may be obtained in Berlin.

The aniline dyes in general possess the useful quality of diffusing themselves in an extraordinary way in water, so that a very small amount colours a very large quantity of water. Moreover, very weak solutions are sufficient to destroy the young larvæ rapidly; and if the solution be made a little stronger, but still very weak, the adult larvæ are destroyed in twelve to twenty-four hours. Besides, while petroleum, being volatile, evaporates readily, the aniline dyes, on the contrary, remain active for a long time. In a large amount of water a solution of one of these two dyes remained active for more than two months, killing the larvæ in fourteen to twenty hours. The action is gradually lost when the water becomes putrid, which, however, in natural clear waters, where the larvæ of *Anopheles* develop, does not occur, or occurs to a much less extent.

Consequently these aniline dyes are of great practical value, especially as they are not poisonous to man nor to mammals, so that the water that contains them in solution can be drunk by cattle.

They are, however, poisonous and deadly to many insects which live in marshy waters and cause damage to crops.

These waters, tinted with the aniline colours, are not in the least injurious to plants; so that this system of disinfection can also be applied to the water of rice-fields.

Larvicide is much more active, and cheaper than gallol. It is sufficient to say that its cost for disinfection per cubic metre of water varies from lire 0·0056 to 0·0012.

In Table XX. we see the effect of various substances on the larvæ and nymphæ of the genus *Culex*, from the most potent to the least efficacious. We see that water saturated with sulphurous oxide kills the larvæ in ten minutes and the nymphæ in twenty-five minutes. The sulphurous water can be readily obtained by burning sulphur and passing its vapour through water. We can also obtain the liquid sulphurous oxide in metal tubes, where it is under high pressure, and by opening the tap it can be passed into the water to be disinfected. Perhaps its manufacture on a large scale will reduce its cost, but at present it is too dear to be employed for this purpose.

TABLE XX.—ACTION OF CULICIDAL SUBSTANCES ON THE LARVÆ AND NYMPHÆ OF MOSQUITOES (C. PIPIENS, C. ANNULATUS).

At the Ordinary Temperature (18° *to* 20° C.).

No.	Substances used	Maximum time required to kill	
		Larvæ	Nymphæ
1	Saturated sulphurous water (SO^4)	10^m–50^m	25^m
2	Potassium permanganate 0·3 + HCl 5 $^0/_{00}$	15^m	1^h
3	Salt water (saturated watery sol. NaCl)	30^m	1^h
4	Chrysanthemum powder (unexpanded flowers)	$1^h\ 15^m$	$1^h\ 35^m$
5	Chrysanthemum powder (second quality)	$2^h\ 30^m$	3^h
6	Petroleum cc. 0·20 in 100 c.m.q. of surface.	4^h	4^h
7	Potassium permanganate 2 $^0/_0$	4^h	8^h
8	Ammonia 2 $^0/_0$	5^h	6^h
9	Oil (very thin stratum, covering the whole surface of the water)	6^h	4^h
10	Petroleum cc. 0·10 per 100 c.m.q. of surface	6^h	6^h
11	Potassium permanganate 1·5 $^0/_0$	6^h	18^h
12	Chrysanthemum powder (unexpanded flowers) 0·006 $^0/_{00}$	7^h	9^h
13	Formalin (formaldehyde 40 $^0/_0$)	8^h	12^h
14	Carburet of lime 10 $^0/_{00}$	8^h	8^h
15	Chrysanthemum powder (second quality) 0·06 $^0/_{00}$	11^h	12^h
16	Lysol 0·1 to 0·5 $^0/_0$	12^h	24^h
17	Milk of lime 10 $^0/_0$	24^h	36^h
18	Commercial chloride of lime 1 $^0/_0$	24^h	48^h
19	" " " 1 $^0/_{00}$	36^h	60^h
20	Potassium bichromate 1 $^0/_{00}$	48^h	60^h
21	" permanganate 1 $^0/_0$	48^h	72^h

Permanganate of potash, which by itself is of little use, with the addition of hydrochloric acid 5 $^0/_{00}$, is effectual in a strength of less than ½ per 1,000.

The saturated solution of salt is very powerful, killing the larvæ in half an hour and the nymphæ in an hour; but this solution, though it can be had naturally in the salines, cannot in reality be utilised in practice, owing to its great cost in Italy, and the large quantity that is necessary. In certain cases sea water, when it is near, is the best and most practical form of disinfectant for the larvæ.

The powder of the unexpanded flowers of chrysanthemums is capable of killing the larvæ rapidly. It is a true larvicidal and nymphicidal poison, and is very soluble in water. We shall see also that, in the form of fumes, it is excellent against the mature mosquitoes.

Petroleum, in the strength of 0·20 cc. per 100 c.m.q. of surface, acts well, killing in four hours both the larvæ and nymphæ; but if it be weaker than 0·10 cc. per 100 c.m.q. it takes six hours, and below this all larvicidal action ceases.

Ordinary oil also acts in the same manner, and on forming a thin layer on the surface of the water it kills the larvæ in ten hours. Both the oil and the petroleum have a mechanical action only, that is, by intercepting the air from the larvæ, which require much oxygen, and therefore come frequently to the surface to breathe. If this stratum prevents the exchange of air they die, but if the whole surface of the water is not covered, space is left by which the larvæ are enabled to gain access to the oxygen in air, and they do not die. So true is this that the nymphæ, which resist chemical disinfectants longer than the larvæ, in water with oil on the surface die in a shorter time than the larvæ (in four hours, see Table XX.). This is to be expected, because they require more atmospheric oxygen than the larvæ, and have to come to the surface more frequently than the latter. One readily understands why, directly the petroleum evaporates, all its larvicidal action ceases.

Formalin, a very powerful bacterial disinfectant, requires not less than ten hours to kill the larvæ and twelve to kill the nymphæ; therefore, this bacterial disinfectant is of little use for our purpose.

Lysol requires twelve hours to kill the larvæ, twenty-four to kill the nymphæ. Caustic lime in a concentrated solution of 10 % requires more than a day!

Summarising the effects of all the substances that have been enumerated for the destruction of the larvæ, we have, in a decreasing order of potency—

Mineral substances—Sulphurous dioxide, permanganate of potash with hydrochloric acid, common salt, potash, ammonia, carburet of lime, sublimate, chloride of lime, and then bisulphites, sulphate of iron and of copper, lime, bichromate of potash, and sodium sulphite.

Organic substances—Vegetable insecticide powders (flowers of *Chrysanthemum; Pyrethrum cinerariæfolium*), tobacco, petroleum and oil, formalin, cresol, some aniline dyes and tar.

Taking into consideration, however, the quantities required, their practicability, and price, all the mineral and some of the organic substances are out of the question, and there remain only the vegetable powders, the aniline dyes, and petroleum.

By cultivating chrysanthemum or pyrethrum plants largely, from the unexpanded flowers of which the powders are made, it is very probable that one will succeed in making the malarious place itself produce a substance which is capable of destroying the mosquitoes which infest it.

The selection of the larvicide for any particular place will depend upon circumstances. It must never be forgotten, however, that the most suitable time for destroying larvæ is the winter and the beginning of spring, when they are fewer in number in the water, and new generations are not being developed. In the winter also it is necessary to insist on the destruction of the mosquitoes themselves in houses or in any place where they are found.

A more perfect knowledge of the habits of these insects, of the places where, and of the time during which they ovulate, will assist in devising means for their destruction, which, even under the most favourable circumstances—that is, when sanitation will have done all that it can do—will be a very difficult undertaking on an extensive scale.

Destruction of mosquitoes.—For a very long time attempts have been made in this direction. In America, for example, besides raising dragon-flies on a large scale with the hope that they would destroy mosquitoes, it has been proposed to light lamps in the places infested with these insects, standing them in a vessel containing a culicidal substance, with the idea of destroying the great number of mosquitoes that would be attracted by the light. But even this means has failed. Again, in all places that are infested by mosquitoes, many culicidal substances are sold—in Italy, for example, *la razzia*, insecticide cones, &c.; but we cannot bring about a wholesale destruction by these means, because they are too costly, and besides, even when used in a room, they more often produce apparent death (lasting for a variable time) than real death of the mosquitoes.

We have directed our attention to this matter, and we have tested many substances, always selecting those which are cheap, so that if found efficacious, they could be used on a large scale. Our experiments are tabulated in Table XXI., and—it is well to note—they were made, for the purpose of comparison, in a very small chamber, and equivalent quantities of the culicides were used.

The substances employed are divided into three categories: *odours*, *fumes*, and *gases*. Among the odours, oil of turpentine and iodoform occupy the first position.

Next come the agreeable odours of menthol and nutmeg; they cause apparent death of mosquitoes in ten minutes, and actual death in from two to three hours.

Camphor stupefies them in four or five minutes, and kills them in from four to five hours.

Garlic stupefies them in a few minutes; kills them in about five hours. This explains the very old custom which is adopted in some malarious regions, by those who work in the rice-fields, of hanging round their neck little bags containing camphor and garlic with the hope of protecting themselves from the bad air; we now know that this prevents the malarial mosquitoes biting them.

Then come substances that are less powerful, pepper, naphthalin, and onion, which, though being very similar to garlic, produces apparent death of mosquitoes after a much longer interval, and never kills them.

As to *fumes*, we would observe first of all that the peasants and shepherds of the Agro Romano unconsciously adopt a prophylactic means against malaria by lighting a fire in their huts. These small and badly ventilated habitations become immediately filled with smoke, and the mosquitoes which are in them either rapidly fly away or become stupefied.

However, as appears from Table XXI., wood-smoke is much less efficient than the fumes of many other substances, requiring a few minutes to stupefy the mosquitoes, but many hours (from twelve to forty-eight) to kill them.

The most efficient culicide is tobacco smoke; this instantly produces apparent death, and actual death in two or three minutes. In malarious places one frequently hears it remarked that 'it is necessary to smoke, in order not to get the fevers;' which is not very far from the truth, inasmuch as tobacco smoke drives away mosquitoes. Nevertheless, a relatively enormous quantity is necessary for killing them, which certainly cannot be produced, even in a small room where many persons smoke, and where they end by making themselves feel ill. Therefore in houses it is preferable to burn larvicide.

and the powder of Dalmatian chrysanthemums or pyrethrums, which in respect to its culicidal action, comes immediately after tobacco. Its fumes do not produce any discomfort. Finally, we have experimented with several other aniline colours which burn, but we have found that none of them equal larvicide in potency.

The fresh leaves of eucalyptus may be utilised and burned, if there is nothing better, especially in railway stations, where, as we have said, these trees are very common. The fumes of quassia wood are slightly less active, killing the mosquitoes in five hours. Pyrethrum powder, which is the chief constituent of many commercial insecticide powders, requires eight hours to kill these insects, but it stupefies them more quickly than the fumes of quassia.

The dried leaves of wild mint, and pitch give off fumes whose action is almost identical with that of quassia.

Then come other substances which stupefy the mosquitoes more or less in the same time as the preceding, or in a few minutes, but which require a much longer time to kill them—namely, from twenty-four to thirty-six hours. These are the fumes of rosemary, the so-called culicidal cones, dry camomile flowers and salvia.

The last culicide is wood smoke; this also causes apparent death in a few minutes, but kills them sometimes only after forty-eight hours.

Some *gases* are more effectual than many of the fumes just mentioned. In fact, sulphur dioxide, hydrogen sulphide, coal gas, formaldehyde, produce

TABLE XXI.—ACTION OF CULICIDAL SUBSTANCES ON MOSQUITOES (C. ANNULATUS, C. PIPIENS, A. CLAVIGER).

No.	Substances used	Time in which death is manifested	
		Apparent	Actual
	I.—Odours		
1	Odour of essential oil of turpentine	1^m	1^m
2	.. iodoform	10^m	40^m
3	.. menthol	10^m	45^m
4	.. nutmeg	10^m	2^h
5	.. musk	30^m	3^h
6	.. camphor	4^m–5^m	4^h–5^h
7	.. leek	5^m–10^m	5^h
8	.. crushed pepper	20^m	6^h
9	.. naphthalin	10^m–35^m	8^h
10	.. Roman wormwood	6^h	24^h
11	.. onion	4^h–6^h	survive
12	.. salvia	—	..
13	.. rosemary	—	..
14	.. dry and fresh basil	—	..
15	.. cinnamon bark	—	..
16	.. asafœtida	—	..
	II.—Fumes		
1	Fumes of tobacco	instantly	1^m–3^m
2	.. larvicide	"	5^m
3	.. chrysanthemum powder (unexpanded flowers)	5^m	1^h
4	.. valerian root	5^m	2^h
5	.. fresh leaves of eucalyptus	3^m–5^m	3^h
6	.. quassia wood	16^m	5^h
7	.. pyrethrum powder	5^m	8^h
8	.. dry leaves of *Mentha Pulegium*	5^m	8^h
9	.. pitch	10^m–13^m	8^h
10	.. dry leaves of basil	2^m–6^m	24^h
11	.. dry rosemary	7^m–12^m	24^h
12	.. culicidal cones	2^m–10^m	36^h
13	.. dry camomile flowers	..	..
14	" dry leaves of *Saturgia hortensis*	..	..
15	.. salvia leaves	8^m–10^m	..
16	.. wood	5^m–7^m	12^h–48^h
17	.. guaiacum resin	12^m	survive
18	.. myrrh	15^m	..
19	.. elemi	..	..
20	.. incense	..	..

TABLE XXI.—*Continued.*

No.	Substance used	Time in which death is manifested	
		Apparent	Actual
	III.—*Gases*		
1	Sulphur dioxide	instantly	1^m
2	Hydrogen sulphide	,,	,,
3	Ammonia	1^m	2^m
4	Illuminating gas	,,	,,
5	Formaldehyde (Trillat's apparatus)	2^m	10^m–15^m
6	Sulphuret of carbon	15^m–30^m	survive
7	Acetylene	—	,,

apparent death instantaneously, and actual death after 1–2 minutes; others, such as sulphuret of carbon, cause apparent death in 10–15 minutes and actual death in 15–30 minutes.

It is curious that the action of acetylene gas is absolutely innocuous to mosquitoes.

Of these gases the most easily procured is certainly sulphurous oxide, which all can obtain by burning sulphur in a room. But owing to its irritating action and its slight diffusibility, in large rooms it is not very useful nor practicable.

It is to be particularly remembered that in general all these odours, fumes, and gases must completely saturate a room in order to kill the mosquitoes.

After performing the above comparative laboratory experiments last summer, we made numerous experiments on a large scale to protect houses, and especially bedrooms, from mosquitoes. And we have found a powder composed of larvicide, unexpanded flowers of chrysanthemums, and valerian root, to be the best for the purpose. Burning 1–2

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tablespoonfuls of it in the evening in a room 36–40 c.m. stupefied the mosquitoes until morning; by burning larger quantities, they were found dead in the morning on the windows and floor. The fumes of this powder are not disagreeable to most people, and if valerian be unpleasant to some, it can be omitted, or its odour can be masked.

In any case the task of the destruction of mosquitoes in the houses of malarial patients becomes at least as necessary as the destruction of pathogenic bacteria, inasmuch as it has been proved that malaria, during that period of the year when the mosquitoes re-enter the houses, is a true domestic disease.

Consequently, *the problem of the destruction of mosquitoes, as a means of antimalarial disinfection, can and should be brought into the practical field of public health. Considering the enormous sums spent by nations and private individuals to protect vines from the oidium, peronospora, and phylloxera, it is to be hoped that something will be done to protect man from the malarial mosquito.*

(*B*) *For Preventing the Penetration of Malarial Germs into the Human Organism.*

Many prophylactic measures can be adopted for this purpose, some of which have been for a long time employed by popular experience.

First of all it is necessary to avoid sleeping in the open air, also absolutely to avoid leaving the house between sunset and sunrise, or migrating during this period from unhealthy places in order to sleep on elevated situations.

It is equally necessary to avoid keeping a light in the room where one sleeps, when the windows are open and unprotected, because the light, as is well known, attracts a large number of insects.

Unfortunately, however, these conditions cannot be rigorously adhered to by people who have to live and work in the Campagna. And therefore a series of *mechanical and chemical* means must be adopted to prevent the bites of mosquitoes.

The first mechanical means is certainly *clothing;* this in malarious places should be, even in the summer, of thick woollen material, similar to that worn in winter. to prevent not only chilling of the body, but also the bites of mosquitoes, which, when they are hungry, bite through thin clothes.

Mosquito nets should also be used round the beds. It is not easy, however, to employ them in such a way as to prevent the entrance of a stray mosquito which has got into the bedroom. And it is therefore necessary, before evening, to try to kill the mosquitoes that get into the bedroom by one of the methods above described.

The best mechanical means is that of protecting *the windows and doors of the houses with a close network to prevent the entrance of insects*; this may consist of simple tulle, which costs little, or of iron wire gauze. However, in the case of people who, owing to the climate and malaria, become apathetic, we are certain that the gauze should be permanently fixed to the windows and to the doors in such a way that they shut automatically.

In order to better protect bedrooms it is advisable also to put up a door on the staircase made of this network. In this way we made, during last summer, an extensive and decisive experiment in the railway cottages between the stations of Prenestina and Cervara on the Rome-Tivoli line, and in a portion of the Rome-Civitavecchia line, which are notoriously the most malarious of the Latial railways. The results were in comparison with the unprotected cottages so obviously favourable, that during the next malarial season we shall repeat the experiment on a more extensive scale. So favourable were they that, in the above-mentioned cottages between Prenestina and Cervara, only those men who were on night service contracted fevers.

Along the same malarious railways we have advised the wearing of a *cowl* similar to that worn by bee-keepers, and *gloves* connected with the sleeves of the coat for those men who have to work at night or in the evening. The cowl would certainly be more useful than the respirators recommended to be worn in malarious places. The men, however, had not the patience to wear them.

There are, in addition, a number of chemical or mechanico-chemical means, which consist in applying on the skin of the hands, face, neck, and other exposed parts *culicifugal ointments*, *soaps*, *or washes*. These in certain places have been in use for a very long time. There are malarious regions where the inhabitants rub their hands and face with the odorous fats of certain fishes or of certain kinds of game; for example: in other places they wash their hands and face with infusions of certain plants, such as quassia, camomile, &c. Analogously a person can use *culicifugal odours or scents on his body and clothing.*

We have already mentioned the custom the workers in the rice-fields have of wearing round the neck a small bag containing camphor and leek, with the view of creating around the body an atmosphere distasteful to mosquitoes. With the same purpose, in many parts of Sardinia, it is the custom to rub the skin of the uncovered parts of the body with a piece of leek.

Recalling what we have said regarding the culicidal and culicifugal actions of odours, we can select several to keep away mosquitoes, and thus prevent them biting. But *in the open air*, especially when it is windy, there is little reliance to be placed in these odours or in the culicifugal washes. Both the former and the latter are, however, efficacious and useful in *living-rooms*, that is in a confined space, where the air is impregnated—I might almost say saturated—with them. Of the various substances used on the skin, the pomade of valerianic acid, and soaps containing extract of tobacco or turpentine, have given the best results for a certain time in the open air. Of these three last culicifugal substances turpentine soap is the best, inasmuch as it has an agreeable odour, does not irritate the skin, and when no longer required can be washed off with a little water.

Finally, where electricity can be easily and cheaply obtained, an electric ventilator placed near the bed may be useful, it being known that mosquitoes avoid strong currents of air.

It remains however to be seen whether, when they are very hungry for blood, and when they are in clouds, the mosquitoes will not overcome their disgust for these culicifugal substances in the various forms of pomades, soaps, washes, and perfumes.

We now come to the

MEANS DIRECTED AGAINST THE PREDISPOSING CAUSES.

1. Against the Organic Predisposing Causes.

We have already seen that the chilling of the body, and all those conditions which predispose to rheumatism, predispose also to malaria in a marked degree.

Therefore the custom of the inhabitants of malarious regions of wearing, when they can, heavy woollen clothing both in summer and winter, especially when they have to go out at night or in the early morning, is a wise one; and thus proper *clothing* comes to be a powerful prophylactic against malarial infection, inasmuch as it protects one from chills.

Is it possible to produce an *artificial immunity* against malaria?

We shall not repeat here what we have already said about natural or hereditary immunity, or of the immunity that may be acquired from previous infection, or of the trials made by us to immunise against experimental malaria. We have seen that among medicinal substances arsenic appears to have some efficacy against an experimental infection.

Long before these investigations were commenced, great prominence was given to arsenic as an immunising agent; in fact one may say that Tommasi-Crudeli was the chief advocate in favour of the prophylactic action of the drug.

Experiments on a large scale were afterwards made with arsenic along the Adriatic railways, at the initiative of the chief inspector, Ricchi, at Bovino, an intensely malarious locality, where the railway staff was divided into two equal parts, one of which was subjected to the arsenical treatment, the other not.

The results are given in the following table :—

Table XXII.—Arsenical Prophylaxis of Malaria.
Bovino Station; 78 Railway Employés.

39 treated with arsenic	36 immune. 3 had mild fevers.
39 not treated	all had fevers.

The arsenic was given in the form of gelatine tablets similar to a postage stamp, each of which contained 1 mgr. of arsenious acid, and the tablets had to be taken in the presence of the local doctor.

From the above table the undoubtedly favourable immunising action of arsenic in respect to malarial infection is manifest.

This experiment was repeated in 1889 in various malarious spots along the Adriatic line on 657 railway men; and it had an equally favourable result, inasmuch as 402 of them were protected from the fevers, 119 had mild fevers, and the remaining 136 were not influenced by the drug.

The arsenical prophylaxis therefore is of some utility.

A quinine prophylaxis, as we have already said, has also been attempted, both with liqueurs which contain a very small quantity of this drug, and with therapeutic doses, that is, giving 1 gramme or 1½ grammes of quinine every five or six days, thus hoping to kill the parasites during the incubation period. But if it be given in small doses it has no effect; if in large doses, as we have said, it cannot, as a rule, be tolerated, especially in summer, even when taken every five or six days.

Perhaps the preventive administration of euchinin, which has not the bitter taste of quinine, and does not produce such severe cerebral and digestive disturbances, will be more feasible. At present, however, it is too expensive.

There is not much reliance to be placed on the substitutes for quinine, nor on phenocoll; on the contrary, much is to be expected from medicinal methylene blue. With this drug and euchinin we intend to make prophylactic experiments on a large scale.

This is what has been done up to now against the organic causes of predisposition to malaria.

We can and ought also to combat the local causes predisposing to this disease. Consequently we shall now proceed to speak of the prophylactic means directed

(2) AGAINST THE LOCAL PREDISPOSING CAUSES.

Here we have to do with a national or State prophylaxis. Although it is true that man can do nothing to influence the seasonal predisposing causes of malaria, on the other hand, he can do a great deal by altering the predisposing physical conditions of a locality. Among these latter conditions it is especially necessary to do away with, as far as possible, stagnant or nearly stagnant collections of water, and, where this cannot be accomplished, to kill the larvæ by placing paraffin or some substance in the water.

The first of these tasks is attained by regulating the surface or ground-water.

Regulation of the surface water.—The surface water may be in the form of rivers, lakes, or marshes, and these can be regulated by preventing inundations, or by drying or putting in motion stagnant or almost stagnant water. Mosquitoes, especially those of the genus *Anopheles*, live only in still or almost still water; therefore, wherever surface water cannot be dried up, it should at least be put in motion. Long ago Cato said that it was necessary *aquam deducere uti fluat.*

And here a number of systems enter into the field of sanitary engineering, which we shall only mention, giving some examples near at hand.

The *regulation of rivers* consists in the prevention of inundations, which, in a low-lying malarious region, give rise to the formation of marshes, and consequently to a local predisposing cause of malaria.

We summarise in the following order the

Methods for Preventing Inundations.

Vegetation on mountains and their slopes.
Steps.
Parapets or traverses.
Repellents.
Rectifications and deviations.
Settling or retaining basins.
Deviators and locks.
Embankments.
Works of defence against washing away of the bed.
Systematisation of the mouths, *i.e.* weirs or locks (Zendrini), or
Dykes in the sea.

We have already stated that woods on mountains and their slopes serve to retain part of the rain-water, and that, on the other hand, on the disforested mountains at every heavy rainfall torrents form on the slopes, which readily cause inundations in the plains.

The so-called *steps* serve to check the velocity of the water, and to keep it back when it descends along a very steep decline.

In the bed of the torrent, at more or less regular distances, obstructions can also be placed, against which the impetus of the water is broken. For this purpose the so-called *traverses* have also been much used since the last century. They are made of the trunks of trees, branches or other impediments, which obstruct the current and act in such a manner that the water carries with it to the plain a smaller amount of earth or sand. Dams and *repellents* act in the same way.

With the *settling basins* and the *locks*, a part of the water, during floods, is made to run into special reservoirs in such a manner that the river will not overflow its banks. Among the *works of defence against washing away of the bed* I mention paving, as has been done in the Adige for the greater part of its course.

As regards the regulation of the mouths of rivers, it is necessary to mention above all that, according to the Tuscan Medical School, to prevent the mixture of fresh and sea water at the spot where the water-courses empty into the sea, Zendrini, the able Venetian engineer, invented apparatus which are still in use and are called *Zendrini's equipoise gates or locks* (figs. 34, 35, 36).

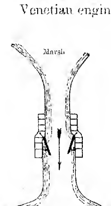

FIG. 34.

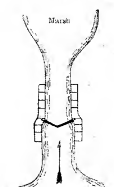

FIG. 35.

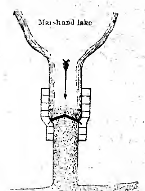

FIG. 36.

When the sea is high it pushes both gates against the river, and the lock is closed; behind these, the river water collects, as it cannot discharge into the sea, until it overcomes the resistance of the sea water, when the gates burst open and it rushes into the sea. And thus from time to time is repeated the closing and opening of these gates.

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Nevertheless, the real efficiency of this system is still a debatable point.

A few words on the *regulation of lakes*.

The water level of lakes frequently undergoes great variations during different seasons of the year, and consequently, between the period of high water and that of low water, the land becomes marshy round the shores. These oscillations may also vary from year to year: for example, the ancient Lake of Fucino underwent during some years very great variations in its water level.

In consequence, in ancient times, and up to the Roman epoch, the necessity was felt of regulating the water of lakes, so as to keep its level more or less constant.

For instance, tradition narrates that, in consequence of the overflowing of the Lake of Albano, in a certain year, the city of Alba Longa, situated on its banks, was inundated and destroyed. A subterranean *emissarium* was therefore constructed to take away the surplus water. Be this as it may, it is certain that this emissarium still exists, and has continued in use from ancient times; a similar one is in use for the Lake of Nemi. Thus in these lakes a constant level of the water is maintained.

Other lakes have an emissarium above ground—the Lake of Bracciano and that of Bolsena, for example; others, finally, have the emissarium partly above and partly in the ground, as Lake Trasimeno, for instance. This lake, undergoing great variations in water level, at certain seasons of the year overflowed its banks, and thus gave rise to malaria. To prevent this overflow, some little time since a large emissarium was constructed, which, in the proximal part is subterranean, and the remainder of its course is above the ground.

A lake may also become completely dried up, as has been the case with Lake Fucino. This lake was entirely surrounded by mountains, one of which impeded what would have been its natural outflow into the River Liris. To overcome this a large subterranean emissarium of stone work was constructed through the mountain, which leaves the lake at its lowest part. And now, and especially during the seasons of heavy rain, the water that would tend to collect in the basin is conveyed by means of canals to the lowest level of the basin, thence to be discharged into the emissarium. This is the famous drainage work completed by Prince Torlonia, on the model of the works carried out by the ancient Romans. This work was planned well, but executed badly, inasmuch as it is too narrow and not sufficiently resistent, so that it soon became obstructed, and matters returned to their former condition.

The *regulation of marshes*, both large and small, is often a very difficult task. It can be carried out in several ways.

One of the simplest, when possible, is that of cutting discharging canals with a sufficient fall. This is the dominating principle of all the hydraulic reclaiming of the Agro Romano. By the law of the Hydraulic Syndicates of the Agro Romano, the latter was divided into basins, and the proprietors of the land united together to open canals for the discharge of stagnant water. Much has been already done in this direction, but much also remains to be done; the maintenance of the canals, which, as is known, owing to the rich vegetation of the marsh plants become very easily obstructed, is frequently neglected. And, besides, the water sometimes has an insufficient fall.

This unfortunately is the great defect of the discharging canals of the Pontine Marshes.

Here the draining off of the water directly to the sea is prevented at the coast by a dune, a true mountain of sand. In very ancient times the so-called Rio Martino (see fig. 25, section of this Rio) was excavated through the dune, but on account of the steepness of its sides it must have been quickly buried.

Consequently, very long canals with gradually sloping sides have been excavated, which traverse the Pontine territory and open into the sea at Terracina. In the midst of the ancient marsh (see fig. 25) a principal collecting canal called *linea Pia*, in honour of Pius VI., was cut. Into this open on both sides transverse canals a mile apart. And then, after collecting the water at the foot of the hills, the River Sisto runs towards the sea dyke, as well as the River Ufente and the River Amaseno from the Lepini Mountains. However, in consequence of a miscalculation it was found necessary to intercept the bed of the River Teppia below Sermoneta. And in spite of this in some months of the year it again becomes marshy. This, therefore, is an example of reclaiming by means of discharging canals, carried out in an imperfect manner owing to the slight fall for the water.

Extensive works have been carried out during late years for the drainage of other large marshes in Italy, such as those of Ostia and Maccarese.

For this purpose the so-called *hydrovorous* machines are used. The idea of this drainage, which is also called *drainage by exhaustion*, is very simple and ingenious. It is employed for marshes whose bottom in some parts is below the level of the sea; consequently it is not possible to cut ordinary discharging canals, there being absolutely no fall for the water.

For this reason they have established these hydrovorous machines, which mechanically raise the water which is at a low level, and discharge it into the water at a higher level; both are then conducted directly to the sea by means of an ancient emissarium which formerly only conveyed the high water of the basin to the sea. The water from the periphery, which, in its turn, would go to the bottom of the basin, is kept back and carried away by canals, which thus separate the high water from the low. Both waters reunite at the emissarium, which conveys them to the sea.

It is a work successful enough from the hydraulic standpoint, and which permits of the initial reclaiming of the land; but from the hygienic point of view, up to the present it has not been of much advantage. All the principal and secondary canals of the basin have little fall, hence the complete, or almost complete, stagnation of the water; and we now know that this is sufficient for the development of generations of mosquitoes.

At any rate, it is true that the *Ravennate* agricultural colony of Ostia, while inhabiting a site where the reclaiming has been most successful, while living sufficiently well as regards food, lodging and clothing, and the hours of work, suffers severely every year from the malarial scourge; and even during the summer and autumn of 1898 not a single member of this colony escaped the fevers, and some have died of them! Therefore up to now no hygienic improvement has taken place there. And yet it was said that these drainage works would save the Roman Campagna from malaria!

The reclaiming in the province of Ferrara, at Codigoro, for instance, and that of the low plain of Fondi, in the province of Caserta, have been done by means of these hydrovorous machines.

The reclaiming by natural and artificial drying of the marshes at Padua, Treviso, Verona, and Rovigo, all of which are regions of mild malaria, has been successful.

The secret of the success of these hydraulic improvements depends on the increased velocity of the water in the discharging canals.

But for an hydraulic sanitation to be complete it is necessary to consider also the

Regulation of the Ground-water.—We state once more that it is especially in this water when it appears on the surface that the larvæ of the malarial mosquitoes prefer to live. Consequently, neglecting to regulate the level of this water may render other very extensive works of hydraulic sanitation useless.

Everything makes us believe that the ancients attained their great success in the hydraulic system of sanitation of this region by regulating the ground-water. Cato and Columella have handed down to us the most precise rules for this purpose. From that time we know that one of the most constantly employed and efficient means for this purpose is *sewerage* or *drainage*, which consists in excavating subterranean canals, with permeable walls and spaces full of air, that act as centres of attraction for the ground-water which surrounds them. If there be a sufficient number of these drains that run in an intercommunicating network through a damp plain in all directions, and if each has a sufficient fall towards a trench or a watercourse, they will drain the land sufficiently well.

These drains are constructed in various ways. The most primitive and imperfect system consists in cutting trenches with sufficient fall at a certain depth, filling the bottom with branches, pieces of wood, maize stalks, bundles of reeds, &c., or with substances which leave spaces to facilitate the percolation of the water. This drainage costs little, but it is not durable, inasmuch as the above-mentioned substances soon begin to decay and are destroyed, and the soil fills up the empty spaces.

When possible it is better to use materials such as broken stones, pebbles, or true lateritious material. In the Roman Campagna, where tufa is easily obtainable, they use large blocks of this stone, and place one along each side and another

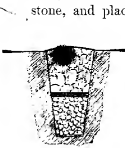

FIG. 37.

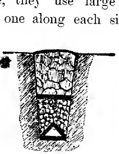

FIG. 38.

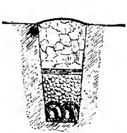

FIG. 39.

on top so as to enclose a triangular space in the trench which acts as a drain. Large pebbles thrown into the bottom of the channel are also used (fig. 37).

When using pebbles and lateritious material, large socles are placed in the bottom in such a manner as to form a drain with a triangular section, into which the water percolates through the fissures between one brick and another, and above these pebbles are thrown (fig. 38). Fissured or perforated drain-pipes are also used (figs. 39, 40).

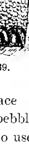

FIG. 40.

It is understood that the drainage quickly and thoroughly removes surface-water, and eventually rain-water, even when abundant; that is, it prevents or diminishes the formation of pools or marshes by rain-water.

By this system of drainage the best sanitation of extensive areas has been effected; in fact, one can say that enormous territories of land in France, Germany, and England, have been reclaimed by this means.

There is also another way for lowering the level of the ground-water. In the Roman Campagna, for instance, this water is very frequently found appearing at the surface, especially at the foot of the hills, forming there local springs. So also the rain-water collecting between the soil and the underlying tufa descends towards the bottom of the hills, and increases the size of these springs, which, collecting in the hollows, form marshes. To dry these a circular trench is made round the base of the hills, which intercepts the water. Other trenches then convey the water into larger ones, until they finally discharge into a torrent or a river.

But it is also necessary *to unite the various springs* which, if left to themselves, readily form small pools of clear water where the larvæ of *Anopheles* live.

Cannot more be done to lessen and regulate here in the Agro Romano the enormous subterranean river which is the principal cause of its malaria?

Di Tucci has proposed the lowering of the lakes (Sabbatino and Laziali), which he erroneously believed were the collecting basins of the ground water. Vescovali conceived the idea of arresting it and conveying it in a large canal excavated above the plateau of the Campagna. In the present state of the science it is difficult to pronounce an opinion as to the possibility of this daring proposal.

It appears, on the other hand, more reasonable and frequently more feasible to regulate all the so-called *marrane* (ditches), embanking and deepening them, or, better, conveying away their perennial ground-water in drains, and adapting the ditches for the reception of the storm-waters. If these ditches were paved, at least in some parts, the work would be more lasting, and certainly hygienically much more useful, than what has been done up to now to remove this principal cause of malaria in the Roman Campagna.

In some regions of Italy the system of *absorbing wells* has been adopted for the draining away of the subterranean waters. These are made in districts where under the impermeable stratum there is one of pebbles, gravel, &c., which readily lets the water pass through. When therefore they bore through the impermeable stratum, in many parts the level of the ground-water is enormously lowered, because a great part of it disappears in the underlying earth.

We have thus mentioned the principal methods for the regulation of water in malarious places.

But after water, air is, as we have said, another local condition predisposing to malaria. To destroy the larvæ and nymphæ of mosquitoes it is sufficient, as we have also said, to limit the free access of atmospheric air to the surface of the water in which these insects live. It is not necessary, therefore, to withdraw all this air. The so-called atmospheric sanitation or covering is sufficient for this object.

Covering. — This consists fundamentally in covering low land with mould.

Coverings with earth are made either with earth which is brought thither by hand, or the floods of rivers are utilised, which, as is known, carry with them a more or less large quantity of mould. That is to say, there are *artificial* and *natural* methods of covering. It is readily understood that only the natural coverings can have extensive application, and it has been adopted principally by Italian engineers, and first by Fossombroni, in Tuscany, for reclaiming malarious territories.

A neighbouring river in flood is allowed to flow over the malarious land, and there deposits a more or less considerable amount of mud. And thus, by utilising the periods of flood, a territory is gradually covered with a stratum of rich mould which has been washed down from the mountains.

This is the ingenious plan for reclaiming Val di Chiana, which was proposed by Fossombroni, and carried out by Manetti and other able Tuscan engineers. It has been for the most part successful. In the same way are being reclaimed the marshes of Grosseto by the floods of the River Ombrone, those of Piombino by the River Cornia, those of Orbetello by the Rivers Albegna and Osa. The process of covering marsh-land in the province of Bologna has been going on in this way for a long time on the so-called *cassa* of Idice and Quaderna. In the province of Ravenna similar improvements are being made by utilising the floods of the River Lamone.

Thus all the lower basin of the River Volturno has been reclaimed by means of the floods of this river and of the Savone.

This system of natural covering therefore has been extensively employed. It takes a long time, sometimes even centuries, but it leads to positive results. It does so, not because it covers the malarious soil with healthy mould, as was said when it was believed that the malarial germ existed directly in the soil, but because in time it increases the distance between the level of the ground-water and the surface of the soil, cutting off or limiting the free afflux of the air. Hence the necessity for levelling the surface of the soil, regulating the surface water, and covering the ground-water. While this natural covering process is going on, the injurious effects it produces have been and are complained of.

Artificial covering is, on the other hand, only applicable for small marshes; for example, it might be used in many places for rendering healthy the pits from which soil has been obtained for making the embankments of railways.

Covering can, so to speak, also be made with *water*. If a stratum of water be made to cover a malarious site, so long as the water remains at a constant level there will be brought about a relative improvement.

The campagna of Mantua affords us an interesting example of this. Near that city the Mincio spreads out into three lakes (the upper, middle, and lower), after which it narrows into a river bed again, and discharges itself into the Po near Governolo. As the level of the water in these lakes was not constant, inasmuch as it rose during the time of floods and fell in the dry season, in the hot months the districts became malarious and the disease extended to the city of Mantua. Then in the time of the Austrian rule, before 1848, the construction of a movable dam at the spot where the Mincio opens into the Po, which would regulate the water in such a way that the waters of the lake would remain at a constant level, was suggested. This suggestion was carried out, and the health of Mantua in respect to malaria was improved. But when, in 1848–49, the Austrians, for purposes of defence, removed this *movable dam*, the fevers reappeared in Mantua, and they ceased again when, after the annexation of the Venetian provinces to the kingdom of Italy, through the insistence of the inhabitants this dam was replaced, without which a vast zone of land around these lakes would have remained marshy.

We have a similar example in the famous Lacus Avernus near Naples.

This lake was certainly pestilential in ancient times, hence its name; and even in more recent times, in consequence of the variations in the water level, malaria existed in the surrounding districts. Then it was proposed to render it healthy, and a stone embankment was built round the lake, and an emissarium established for the purpose of keeping the water at a constant level, and by these means the surrounding lands were no longer inundated.

This submersion in certain cases is only relatively beneficial, and its real value will have to be tested in the light of the new theory regarding the origin and propagation of malaria by means of mosquitoes.

Thus perhaps will be explained what seems to be a paradox, namely, that the suppression of an epidemic of aquatic origin is brought about by the presence of water!

Certainly the natural covering, utilising the inundations of rivers, is a true method of sanitation, because in this case the covering material is earth, and in the place of a marshy soil a dry, and therefore perfectly healthy, soil is gradually being formed.

If the basin to be filled up is large, and the river is only slightly muddy, this improvement takes place very slowly, but its effect is certain and definite. Thus, for instance, the sanitation of Val di Chiana has now for many years been partly finished, and its good effect is stable and lasting.

When dealing with the sanitation of the marshes of Ostia and Maccarese this project of covering has also to be discussed. There the conditions are very favourable, inasmuch as these marshes are situated on either side of a large and particularly muddy river, namely, the Tiber, which, even when it is not in flood, carries with it a large quantity of fine sand, and when in flood its waters are extremely muddy.

Unfortunately this system has not been adopted, because it requires a long time; it has been calculated that it would require thirty years; and as, even after 1870, the prejudice that the malaria of Rome depended on these littoral marshes still existed, it was said that the new capital of Italy could not certainly remain malarious for thirty years, and the more rapid method with hydrovorous machines was adopted. But unfortunately this method has not been successful, and that prejudice has already cost many millions of francs and also many lives.

In any given case the decision as regards the method of hydraulic sanitation to be adopted must be guided by the new epidemiological facts concerning malaria.

The essential requirement for all systems of hydraulic sanitation is that they do not leave a way for the larvæ and nymphæ of the malarial mosquitoes to live in the water.

Covering with mould fulfils this requirement, when it raises and levels the marshy soil, and thus removes the water and the free access of the air. More directly, drainage, by removing the water, and allowing the direct access of the air, is excellent for preventing the development of the larvæ.

And, in fact, both are equally efficient methods of hydraulic sanitation against malaria.

All the other systems with open discharging canals are good, or the reverse, according as the velocity of the water permits or does not permit the eggs and larvæ to remain and develop in it; hence the variable results that are obtained, namely, good, indifferent, or negative, according to circumstances.

We have said that from direct experiments it has been shown that a velocity of 63 mm. per second is compatible with the presence of the larvæ of *Anopheles*.

These experiments, however, must be continued, inasmuch as they have revealed the secret of the above-mentioned contradictory results, and they will enable us to formulate schemes for sanitary improvements in the future. For the present we can say that the theoretical minimum velocity of 0·20 mm. per second should be always obtained and maintained in practice in the canals and in their secondary and terminal branches. Otherwise they should be covered, and thus converted as much as possible into drains.

Nevertheless, no hydraulic improvement, even when carried out on the most approved system, can ever be completely successful unless it is made complete by means of the so-called **agrarian sanitation**. Before a district can be brought under cultivation many hydraulic works have to be carried out; the surface and subsoil waters have to be regulated by discharging canals and drainage, because many plants will not grow in damp soils.

These agrarian hydraulic works are the complement of the more important works of hydraulic sanitation. Even the levelling, ploughing, &c., of the soil, contribute to render it healthy by making it more permeable to the water.

Of all the cultures, therefore, the best is what is called intensive culture; which is also one of the most remunerative when it can be adopted. Tommasi-Crudeli has observed that in many malarious localities intensive cultivation has sometimes attenuated, sometimes suspended, and sometimes perhaps even suppressed, the production of malaria.

In malarious sites dry cultures are advisable; *vice versa* artificial meadow-lands are not advisable, or at least they should be managed by certain rules according to which the water in the channels should not be allowed to become stagnant, but, on the contrary, should be made to run in such a manner as to prevent the growth of the palustral vegetation and to sweep away the eggs and larvæ which may eventually be contained in it. For this purpose the constant supervision of the channels would be necessary.

Rice-fields in malarious places should be absolutely condemned, until a cheap larvicidal substance is found which is not injurious to the plants, as, perhaps, according to our experiments, are the best of the above-mentioned larvicidal dyes (p. 197).

Is it advisable to plant trees, and in general is it advisable to maintain or plant woods, in malarious sites?

That the planting of woods is not a protection against malaria has been demonstrated by the example already recorded of the Tre Fontane, where in spite of the eucalyptus wood, which has grown vigorously, this disease still remains.

Imagine then what must happen in those woods along the littoral, inhabited by myriads of mosquitoes and by all kinds of insects, with numerous marshes even in the height of summer! Here disforesting would be a real hygienic improvement, inasmuch as the land could be levelled and drained, and thus placed under cultivation.

In fact, there are localities round Rome where malaria used to be rife (Conca, Campomorto, for example), which to-day are more healthy, because the trees have been cut down to a great extent and the ground cultivated. The same has happened, as we have seen, at Cisterna.

Now a few words on **urban sanitation against malaria.**

There are towns immune or practically immune from malaria, although they are situated in the midst of a pestilential region, such as Grosseto, and more especially Rome.

Here in Rome the first great sanitary improvements were made in the epoch of the kings; the justly famous *Cloaca Maxima* at first served only to dry the two *Velabri*, like an enormous drain made of colossal blocks of tufa, which were not cemented, and between which the water percolated. It was only later that it was also used as a sewer for part of the city.

In the same way a similar form of drain was also excavated for draining the Caprea marsh; and successively all the sewers of ancient Rome were used for the same purpose. When these were abandoned and buried in the Middle Ages, the ground-water reappeared on the surface, and malaria, with other pestilences, prevailed in the deserted city, whose population was reduced to a few thousand inhabitants. After the Renaissance, Sixtus IV., Alexander VI., Gregory XIII., Urban VIII., and Paul V., more for the object of drainage than for sewerage, repaired the old sewers and made new ones, and these are still in use to-day. They are not impermeable sewers, but act like sieves in which the water of the fountains runs, and into which the subsoil-water percolates in such quantities that the sewerage which is passed into them in recent times is hardly noticeable.

Hence all the sewerage of Rome, ancient and modern, in the valleys of the city, forms an immense work of hydraulic sanitation. Its sanitary effects were immediate and lasting. Rome since then has been one of the healthiest of the large cities.

In our time also we have experienced the beneficial effects of a sewerage system which was made for the purpose of draining away the ground-water. Thus the reopening of the *Cloaca Maxima* has rendered the *Forum Romanum* healthy; the construction of a new sewer under the *Colosseum* has rendered this amphitheatre healthy, and the sewer of the Via del Babbuino has freed the houses situated under the Pincio from the fevers.

If to this be added the paving and the extension of the streets, we can understand how one can have, by the withdrawal of atmospheric air and the rapid carrying away of the rain-water, a very healthy city surrounded by a pestilential district, inasmuch as the mosquitoes cannot fly, as we have said, to great distances, and the suburban houses, and perhaps also the walls of the city, are to a certain extent a protection from the insects of the surrounding Campagna. Finally, a town can also be healthy in an intensely malarious territory if it be built in an elevated position, particularly when the site rises perpendicularly from the underlying Campagna. With this hygienic aim, which to-day can be perfectly explained by the habits of the mosquitoes, the villages and small towns of the Roman province since the Middle Ages have been built, as we have said, upon elevated sites, all, or almost all, of which are precipitous.

We shall now say a few words about the **sanitation of the malarial industries** (fish-ponds, peat bogs, salines, railways). We have mentioned that the railways have helped to maintain and create local conditions favourable to the development of malaria, both by the excavation of pits (*cave di prestito*, p. 147) into which the subsoil-waters drain and form marshes, and also by the embankments or terraces which intercept the watercourses which tend to discharge themselves into the valleys. Frequently these railways have been constructed without any regard to hygienic principles, and without even thinking how to avoid aggravating the state of things in reference to malaria which exists in a great part of the Italian territory.

Therefore the first laws of sanitation in Italy should be directed to the sanitation of the railways, where, at little cost—filling up many of the pits, for example—a large number of poor people would be protected from malaria. And as to the railways to be constructed in the future, the law should make a decree that no malarious foci be formed or increased by their construction, even where malaria no longer exists or is not intense.

The sanitation of fish-ponds will become possible when a culicide which is not poisonous to fish can be used with little expense.

The sanitation of peat bogs can be brought about by means of pumping machines that exhaust or put in motion the waters which have no natural outlet.

As to the sanitation of the salines it is not necessary here to repeat what we have already said at pages 79 and 145.

We have thus seen how the physical or local predisposing causes of malaria can and should be combated.

We shall next see what can and ought to be done

(3) AGAINST THE SOCIAL PREDISPOSING CAUSES.

I shall briefly mention the social reforms or laws which are most indispensable for correcting the terrible epidemic predispositions to this scourge.

We begin with **alimentation**

The Romans in their most flourishing epoch established with much equity and wisdom the treatment of the slaves who worked in the Campagna. As Mommsen says: 'The slaves, and even the intendants, received from their master at stated times, and in pre-established amount, as much as they required for food, clothing, and hose, with the obligation of maintenance. To each of them was given a certain quantity of wheat, which he had to grind himself, besides salt and condiments, or olives and salt fish, wine and oil. The quantity of the food supplied depended upon the nature of the work, in consequence of which the intendant, who worked less, received a smaller ration than the slave.'

Therefore, the great principle that the alimentation should be proportionate to the amount of work was even then recognised!

Nowadays, on the contrary, no prophylactic measures are instituted from this point of view. With difficulty, and solely for the application of the law of the agrarian sanitation of the ten-kilometre zone round the city, a regulation of rural police and hygiene was issued on August 26, 1885, in which some of the articles refer to alimentation. One of them, Article 41, is very just, which prescribes that 'the food exposed for sale or given by the proprietors or tenants of the farms to the workmen, if unwholesome, shall be immediately seized and destroyed, if it cannot be, at the request and care of the proprietor, innocuously utilised for other use than human consumption, with the directions and guarantees which in individual' cases shall be deemed necessary by the authorities.'

Then come Articles 4–5, dealing with luxuries with regard to meat, which is only known among the workers of the Agro Romano as that obtained from dead animals. They prohibit trichinosed meat, as if trichina existed among us; and other meats are also prohibited, for instance *abbacchi* (very young lamb) and lamb not fully developed, whose flesh is too fresh! Would that the peasants could eat these kinds of meat!

We now come to **clothing**.

As Mommsen has stated, in the Roman Campagna from ancient times the people have clothed themselves with wool, even in the summer. This kind of clothing was provided for the slaves, and Columella justly insisted that it should be given to them in a good condition.

But to-day, to provide sufficient food and clothing for the peasants working in malarious places, a law is necessary which would fix, above all, the *minimum wage* to be paid to them. At any rate co-operative supply associations, or similar institutions, should insist that the greatest possible proportion of the daily wage be expended for food and clothing.

The ancients also recognised the importance of proper **housing** as a prophylactic measure. It is certain that among the means adopted by them for combating malaria, great consideration was given to the construction of country houses. Two students of antiquity, Augusto Castellani and Efisio Tocco, have studied the question of the housing of the Romans in the Agro. We know how the Roman houses were constructed, splendid typical examples of which we see at Pompeii. The house was a kind of sanctuary, surrounded by a wall, without or with few

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windows communicating externally; the doors of the separate rooms opened into one or two courtyards, which were freely open above.

In the same way, in the houses of the Campagna the enclosing wall was high, and in the centre was a large courtyard into which opened the doors and windows of the house, while communication with the outside was effected by means of one large entrance door; the house was ventilated only from the courtyard. This, perhaps, does not represent an ideal form of ventilation, but it would constitute even to-day a good system as regards a prophylactic measure against malaria, because mosquitoes cannot rise easily much above the ground, and consequently they would have greater difficulty still in invading the rooms of a house constructed in the mode just described.

After the Renaissance, when the agricultural revival took place, of which we have spoken, large villas, with annexed buildings, were constructed from 1600 to 1700, which to-day are often used for the most humble purposes, and which are frequently squalid and almost in ruins. There were 64 disused houses in the Campagna in 1871, and 231 in 1881. There has therefore been in our time a falling off in the numbers of habitable dwellings.

When a new house is built, or an old one restored, it is done as if it were situated in a very healthy locality, whereas habitations in malarious places should be built with special precautions. First of all, they should be erected on the highest site possible, and consist of at least two floors, the ground floor being used for storing agricultural implements, &c., and, if necessary, for stalls; the kitchen and bedrooms should be on the second floor, where the insects are less liable to gain access.

There are already many examples of this type of house, for instance along the Rome-Monterotondo railway. Besides the two floors, those houses in which several families live have an outside staircase, which leads to a landing that runs along the whole length of the second story, on to which the doors of the separate apartments open. It would be even better if the doors of the rooms opened into a hall and not directly on to the landing.

The windows should be placed as high as possible, and should not be very large; they should, however, be always protected with a close wire netting. The netting should also be placed in the doorways, or at least, when this is not possible, on the inner staircase, in order to isolate the bedrooms more effectually.

In 1875 Dr. Balestra proposed that some cheap and healthy wooden houses of various sizes should be constructed in localities much infected by malaria, which could be taken to pieces and easily transported to any place desired. He suggested that the windows should be permanently closed, and ventilators arranged in such a way that they allowed only pure air to pass through them, that is, air which has been filtered, and consequently is free from miasmata or, as we know now, from mosquitoes. By substituting for the closed windows a wire network, and by similarly protecting the door in such a way as to prevent the insects from entering, these wooden houses would be very suitable for protecting the peasants from the fevers in places where there are at present no houses, or where they are scarce or are unsuitable for this purpose.

Finally it is advisable not to have trees around houses in malarious places. During the day they harbour mosquitoes, which in the evening get in through the windows, especially when the rooms are lighted.

It is desirable that our architects should study this question, and design houses suitable for malarious places, guided by the new theories and by the old traditional experience of our peasantry regarding malaria.

The regulations for the public health of the Agro Romano lay down that, above all, every farm must have sufficient habitations for the people who work there. This law should absolutely prohibit what occurs at harvest time, when, owing to the large numbers employed, a great part of them have to sleep in grottoes or in the open air. The regulations speak of 'habitations constructed on elevated sites on dry ground,' and this is right; but then follows a strange prescription: 'in a place protected from the injurious influence of unhealthy winds,' as if a house built on a high place would not be beaten by all the winds, and as if some winds were still considered unhealthy in the sense Lancisi believed they were.

'When the soil is humid,' says the same law, 'works for the discharge and drainage of the waters must be carried out,' and this is quite right; but then comes this strange order: 'Trees must be planted between the houses and the malarious land,' and then again: 'The houses must be built at a distance not less than 200 metres from cemeteries,' when it is known that our cemeteries are in no way injurious to the health of the residents who live near them.

There are then some good Articles: 'The house must be protected from damp, provided with potable water; the rooms must not be less than 3 metres high, and each person must be allowed a space of at least 15 c.m.;' all excellent things, but they have one fundamental defect—they are not enforced.

The hygienic regulations of the Municipality of Rome also contain articles relative to country houses, sufficiently good, and very comprehensive; for example, it is laid down that the dwellings, commencing with the ground floor, must be raised as high as possible; and when the ground floors are used as habitations, they must be raised at least 2 metres above the ground. Beyond these, one may say that there are no other special regulations relating to this question.

We next come to the **legislation relating to work in malarious places.**

If we recall for a moment what we have said on the agricultural works here in the Campagna, and on the unprotected state of the poor peasants, left to the mercy of him who most profits by them, one readily understands the urgent necessity of a law which would regulate this work, so laborious, difficult, and dangerous. The first step should be that of abolishing the impoverishment of the workers by the so-called *caporali*. But unfortunately no one thinks about it!

We have only a law on the *cultivation of rice*. This law dates from June 12, 1866; the first and fundamental article says: 'The cultivation of rice is permitted at the distances from the blocks of houses and under the conditions prescribed in the interest of public health by special regulations that, after consultation with the communal and sanitary authorities of the province, are determined by the provincial councils and approved by the King, after consulting the Superior Council of Health and the Council of State.'

It is, therefore, in the power of the provinces to control the cultivation of rice by means of local regulations. Now, in these regulations we find articles which vary very much according to the humour of the provinces, especially as regards the minimum distances from the rice-fields within which houses are permitted to be inhabited. We have seen (page 82), from the studies of Professor Riva and of Dr. Ambrosi on the zone of influence of the rice-fields, that this sometimes may be as much as 3, 4, and occasionally 5 kilometres. Now the local regulations of the province of Cremona, which, perhaps, are the best of the kind, establish a minimum distance that varies according to the number of the inhabitants of the individual blocks of houses. These distances are given in the following table:—

TABLE XXIII

Distance in metres	3,000	2,000	1,000	400	200
Number of inhabitants	Above 10,000	10,000 to 3,001	3,000 to 301	300 to 31	30 to 1

While for 10,000 persons and more the houses must be at least 3 kilometres distant from the rice-fields, those for 30 persons need be only 200 metres. As a rule, this curious distinction is made in all these local regulations, as if the life of persons has a different value according to whether they live in a large or small community. These regulations, instead, ought to have established that even a single isolated house, and in general a single habitation, must be outside the zone of injurious influence of the rice-fields, that is at least 2 to 3 kilometres distant from them. The Internal Sanitary Law of the Two Sicilies of 1820 very wisely ordered that 'the cultivation of rice shall not be permitted at a distance less than two miles both from the communes and the public roads.'

In the regulations for the cultivation of rice the hours of work are also fixed; and, for the most part, the axiom of not commencing work before sunrise, and of leaving off an hour before sunset, is respected.

It being, however, such laborious work, a greater limitation of the hours of labour is necessary; and it is especially desirable that the labourers should leave off work earlier, inasmuch as the mosquitoes begin to bite some hours before sunset. In this respect the labourers on the Pontine Marshes, who leave off work as early as possible, and return to their hills in the evening before sunset, are better treated.

There is also in the regulations of the province of Cremona an article relative to habitations, which establishes that they must be provided

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with potable water, that the rooms must be dry and well ventilated, with sashes and glass in the windows. These are good regulations, especially that of the glass (network would be better) in the windows, as a prophylaxis against malaria.

In general, however, it may be said that our legislation on the cultivation of rice is defective both in the fundamental law and in its practical application. It does not take into consideration the geographical division of malaria into zones of severe malaria and zones of mild malaria. If the cultivation of rice can be with due limitations and precautions tolerated in the zones of mild malaria, it should be *absolutely forbidden* in the provinces of Italy situated below the isotherm + 15°, where severe malaria prevails.

And even in the localities of mild malaria the cultivation of rice should be permitted only where there are marshes in low-lying lands which cannot possibly be drained, and where no other kind of cultivation is possible. Thus its cultivation would be limited, and it would be all the better for public health, because we remember that in many instances malaria has disappeared where the cultivation of rice has been given up.

To regulate the *maceration of textile plants* we have, in the sanitary law of 1888, an article (article 37) which decrees that this maceration can only be carried on under certain conditions of place, time, and distance from inhabited houses; conditions which must be determined in each province by the local public health regulations or by special regulations.

In a supplementary article to the general sanitary law, published in 1890, it was decreed that those communes in which the maceration of rice was carried on were obliged to prepare within a year these special regulations or to add the relative chapters on the maceration of textile plants to the local public health regulations, indicating in which places, at what distances, and with what precautions this industry must be practised. The same article says that the communes must take specially into consideration the banks, the exchange of water, and a convenient outlet for the used water; and that they must impose a minimum distance of 200 metres between the place of maceration and the houses. If the communes declined to comply with these regulations, the prefect would intervene, on the advice of the provincial Council of Health.

The local regulations of the commune of Rome, in agreement with what has been established in the general sanitary law, decree that 'the maceration of textile plants is permitted only in the open Campagna, at the distance at least of 200 metres from the houses, canals, wells, or other reservoirs of potable water, when it is carried on in running water, and is not that which feeds the aforesaid canals, wells, or reservoirs. The maceration must take place exclusively in suitable tanks with impermeable bottom and sides, according to the project approved by the mayor.' But if this maceration be a cause of malaria (which certainly has not been demonstrated) the 200 metres are not sufficient to protect the houses, nor is slowly running or stagnant water sufficient.

But, besides this, cultivation of hemp and flax does not exist in the Roman Campagna.

We shall conclude with a few words on the *laws on agrarian improvements*, and on the so-called *internal colonisation.*

Of these improvements several have been made according to the various laws that have been approved from 1882 onwards. In Venice, for instance, the land has been successfully reclaimed on a large scale ; in the rest of Italy there is a great deal to be done, inasmuch as there still is, as we have already said, an enormous number of marshy hectares to be drained. Unfortunately some reclaimed lands, like those at Ostia and Maccarese, are anything but hygienically successful, and unfortunately also the last law will fail if the modern researches are not taken into consideration.

For the execution of these works, some conditions relative to the health of the workers have been included in the law of September 7, 1887. Article 92 says that ' in approving the project the rules necessary : as to the seasons during which the works have to be stopped ; the hours of the day during which the workmen must abstain from work ; the habitations that must be built to house the workers, shall be established.'

Article 93 says that 'regulations of the same kind can at any time be sanctioned with prefectual decree in respect to the maintenance of the reclaiming works.'

But, besides the regulations for the seasons, the hours of work, and the habitations, it is also necessary that other regulations—for the selection of the individual workers, for example—should be established. These workers should be selected from the families most resistent to malaria, and a doctor should exclude (especially by the examination of the blood) those who have even the least trace of malarial infection, inasmuch as with their recurrent attacks they are dangerous to those with whom they live. Regulations should also be made with reference to the sheds for working in. The shed, the centre of activity, should be situated on an elevated and healthy site, or at least on a site properly drained, so as to eliminate the surrounding stagnant or almost stagnant waters as much as possible. A minimum wage should also be established, and should be converted into food and clothing without the intervention of middlemen.

The cases of fever, also, should be included with the cases of accident through work; and the patients should be treated, and even taken to sanatoria, or to healthy places, until complete convalescence is established, at the employers' expense. This would also prove a useful general prophylactic measure.

In all ages (see pages 1–12) attempts have been

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made to colonise malarious places, but these attempts have frequently failed.

Experience has proved, over and over again, that the error lay in sending to places of very severe malaria agriculturists accustomed to live in healthy regions. We have already spoken of the annihilation of the Venetian colony introduced into the Pontine Marshes. A similar disaster has happened recently to families of agriculturists from the Marche brought here to live in very unhealthy places along the littoral.

Man cannot combat against this terrible enemy malaria, if, first of all, the land has not been thoroughly drained and kept in this condition. When this has been done, then the colonisation which leads to the agrarian improvement can be attempted.

This reclaiming of the land has been tried in various places by prison labour. For example, a colony of this kind was employed at Castiadas, in Sardinia, and the results have been fairly good. Another was tried near Rome, at the Tre Fontane, but it had to be removed because all fell ill with malaria. And yet, without doubt, prisoners are working under better conditions as regards clothing, food, housing, and hours of labour, than the peasants of the Agro Romano.

With all the more reason, therefore, attempts at colonisation with people from healthy places, made without any criterion but that of profit, should be prohibited by law, because a colony of men transported from a healthy region to a very pestilential one absolutely cannot stand it. Some economists maintain that malaria does not in the least prevent the intensive cultivation of land, and consequently its colonisation. But history teaches us that if man has frequently sacrificed himself for the redemption of unhealthy places, it is nevertheless very true what Varro says, that unhealthy lands can only be cultivated at the risk of the life of the worker and the substance of the owner. Before the cause and the prophylaxis of bovine malaria was discovered, the industry of dairy farming has been here many times attempted, but always in vain. The same can be said of the many fruitless attempts at colonisation. And until we shall be able to discover a complete prophylaxis for man as we have done for milch cows, it will be necessary not to accept those ideas so readily spread abroad on the so-called internal colonisation, because a malarious district cannot be easily or quickly rendered healthy. And yet there are people who loudly declaim against the enormous extent of land uncultivated; but in reality in Italy, with our industrious and hard-working peasants, the only zones left uncultivated are those where no person can live.

Certainly the State ought to promote more than it does works of hydraulic sanitation. When it has done this, then colonisation can be attempted, proceeding step by step from reclaimed land to land still unhealthy. And this is actually being done in the Agro Romano, inasmuch as from Rome and from the Castelli Romani and from Velletri the zones of cultivated land are being extended towards the Campagna. And it is to be hoped that within no distant time these zones reclaimed by human industry will reach at least that high and marvellous part of the Agro Romano which joins the capital with the splendid Castelli Romani.

The colonisation ought to be extended also on the hills situated above the valley of the Tiber, especially on the right side, and houses should be built on these hills, even in the valley itself; in like manner the inhabited centres or country villages that have always existed, since the olden times and the Middle Ages, on the highest and healthiest parts of the Campagna, should be enlarged.

To do this, however, it will be necessary to abolish that agrarian feudalism by which the land remains in the hands of a few who have not, owing to self-interest or to dislike of innovation, any desire to change the ancient system of cultivation. Unfortunately such a state of feudalism could not be changed here, as it was in northern and central Italy at the time of the communes and afterwards during the French revolution. The Italian revolution has certainly made it worse, secularising the ecclesiastical properties, and substituting for the religious communities capitalists or speculators who acquired the lands at a low price and make use of them for their own profit.

Then the law on the agrarian sanitation of the Agro Romano has not had the courage to break up the small but omnipotent band of proprietors, privileged more than they deserve, nor to improve the agrarian contracts, nor to prevent the organised spoliation of the tillers of the soil. It consequently has been a dead letter and will remain so, as long as private property possesses the right of *uti et abuti*, and with impunity remains the greatest enemy of public health.

Therefore it is more than ever urgent that hygiene should dictate to the legislature, and that the latter should put in force an easy and ready prophylaxis for our poor peasants living in malarious places. Then the problem of the sanitation of many fertile lands will approach solution. For the present at least, the treatment for the disease should be immediate and efficacious by means of quinine obtained free or at a very low price, which should be fixed by the creation of a State monopoly.

Finally, a last word must be said on **education** as a prophylactic measure against malaria.

It is certain that when the sources of infection of this, as of every other avoidable disease, the life-history of the infective germs in the environment, the vehicles, the mode of penetration, and the various prophylactic means are known, much will have been attained. Knowledge and power are necessary for combating epidemic diseases; but the knowing how to combat them is a great deal. And as the individual prophylaxis in malaria is very often practicable and efficacious, one understands how the spread by means of education of the most certain facts of the new epidemiology and prophylaxis, the combating of the old prejudices which dominate among the toilers of the soil, will be so many preventive measures against a scourge that in every way should be combated for the good of humanity, of civilisation, of business, and, in a word, of human progress.

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